UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

ASTELLAS INSTITUTE FOR REGENERATIVE MEDICINE, Plaintiff, v. IMSTEM BIOTECHNOLOGY, INC., XIAOFANG WANG, and REN-HE XU, Defendants.	C.A. NO. 1:17-cv-12239-ADB

ASTELLAS' FINDINGS OF FACT AND CONCLUSIONS OF LAW

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Abbreviation	Term
’956 patent	U.S. Patent No. 8,961,956
’321 patent	U.S. Patent No. 8,962,321
’551 patent	U.S. Patent No. 9,745,551
ACT, ACTC	Advanced Cell Technology, Inc. (predecessor-in-interest to Astellas)
Astellas	Astellas Institute for Regenerative Medicine
BIO	(2’Z,3’E)-6-Bromoindirubin-3’oxime, a GSK3 inhibitor
BM-MSC	Bone Marrow Mesenchymal Stem Cell
EAE	Experimental Autoimmune Encephalitis or Experimental Allergic Encephalomyelitis, an animal model of Multiple Sclerosis
EBs	Embryoid Bodies
ESCs	Embryonic Stem Cells
GSK3	Glycogen Synthase Kinase 3
GSK3i	Glycogen Synthase Kinase 3 Inhibitor
HB	Hemangioblast
HB-MSC	Hemangioblast-derived Mesenchymal Stem Cell
hESCs	Human Embryonic Stem Cells
IL-6	Interleukin 6 (a cytokine secreted by MSCs)
ImStem	ImStem Biotechnology, Inc.
IND	Investigational New Drug Application
MA09	A human embryonic stem cell line developed at ACT
MA09-MSC	An HB-MSC generated starting with MA09 human embryonic stem cells
MS	Multiple Sclerosis
MSCs	Mesenchymal Stem Cells
Patent Office	U.S. Patent & Trademark Office
PCT	Patent Cooperation Treaty (a type of international patent application)
SCRMI	Stem Cell & Regenerative Medicine International, Inc. (predecessor-in-interest to Astellas)
T-MSC	Trophoblast-derived Mesenchymal Stem Cell
UConn	University of Connecticut

All emphasis added unless otherwise noted.

I. INTRODUCTION

As the evidence at trial made clear, this is a case about the invention of a new type of stem cell with breathtaking potential, the HB-MSC. It was Drs. Kimbrel and Lanza who conceived of, worked tirelessly on, and first created the HB-MSC. And they did so before Drs. Xu and Wang had ever ***heard*** of HB-MSCs. All of this is undisputed.

Yet Defendants want to be named as inventors not only on the '551 patent, but on ***Astellas'*** fundamental HB-MSC patents. Why? Solely for suggesting things that were not only already known in the art, but were ubiquitous. Such as for suggesting that Astellas' MSCs could be used for treating MS, when the art was replete with using all sorts of MSCs to treat MS. For suggesting that MSCs could be mitotically inactivated, when myriad references taught the exact same thing. For measuring IL-6 levels, when Defendants admitted—in a sworn grant proposal—that IL-6 was ***already*** a promising target (and where it is undisputed that Dr. Kimbrel measured IL-6 levels ***first***). And for suggesting that Astellas' MSCs should be compared to conventional, BM-MSCs. Three out of four of which Defendants correctly admitted, in sworn interrogatory responses a year and a half into the case, were never inventive in the first place.

Astellas' evidence, including dozens of journal articles, the testimony of preeminent experts, and Defendants' own patents, grant applications, and internal documents, established not only that the above suggestions were obvious (and therefore not inventive), but were the ***most obvious*** things to do with a new type of MSC. How did Defendants respond? By asking the Court, time and again, to ignore contemporaneous evidence in favor of litigation inspired fantasies that ranged from merely unsupported to farcical. In one unfortunate example, Dr. Wang accused Dr. Fortier of "misleading" the Court for making the same statement he himself made in a sworn grant application and the '551 patent. In another, Dr. Wang testified that when he said the EAE model was "easy," he actually meant "not easy." In another, Dr. Wang relied on notebook entries on

direct to show when he had done certain work, then reversed course 180° on cross, after realizing they betrayed a lack of creativity or effort. And in another, Dr. Wang tried flippantly to explain away his sworn interrogatory responses based on a lack of time to review a handful of patent claims—one sentence each—in the first year and a half of the case, despite his earlier testimony that the case had been all-consuming. At that point, Dr. Wang was making it up as he went along.

This case epitomizes why the law on inventorship requires corroboration—hard evidence—and disregards interested inventor (or putative inventor) testimony. Here, the documents are decisive and dispositive. They establish that Defendants came nowhere near establishing joint inventorship of Astellas' patents, much less by clear and convincing evidence. And, they establish that Astellas ***did*** present clear and convincing evidence that Defendants should not be joint inventors of the '551 patent. Finally, they establish that Defendants committed unfair trade practices under Massachusetts law. This Court should find for Astellas across the board.

II. PROPOSED FINDINGS OF FACT

A. Astellas Developed The HB-MSC Method Before The Collaboration

1. Astellas developed the method of making HB-MSC disclosed and claimed in Astellas' '956 and '321 patents before any interaction with Defendants. Tr. 6-52:2-25, 10-30:6-18, 10-36:6-14, 6-178:11-180:19. Dr. Lanza had the idea to make "immunomodulatory MSCs" using an HB intermediate by September 20, 2009. Tr. 1-100:1-103:10; TX-38 (email with article on Pluristem's MSC program attached). Dr. Fortier opined,[1] after reviewing relevant documents and testimony, that Dr. Lanza came up with the idea of using HB-MSCs to treat autoimmune diseases, including MS, before Drs. Wang and Xu allege to have come up with it. Tr. 3-49:18-

[1] Defendants, in contrast, asked their experts to ***assume*** that Drs. Wang and Xu came up with the ideas they allege, rather than perform an independent inventorship analysis, and withheld nearly all internal documents from their experts. Tr. 7-57:19-25, 7-103:3-10, 7-55:10-20. Indeed, they didn't even invite their expert, Dr. Perry, to observe their testimony. Tr. 8:57:23-58:6.

50:24. While Defendants dismiss the contemporaneous evidence corroborating Dr. Lanza's September 2009 conception, they do not dispute that by Fall 2009, Dr. Lanza reviewed a publication about potential therapeutic uses of MSCs, including for the treatment of autoimmune disease and MS, and with that article in mind, directed his team to begin work on making HB-MSCs, and Dr. Kimbrel did so. Tr. 1-100:1-103:10, 2-17:6-21:13; TX-38; TX-EZ.

2. As Dr. Lanza explained, his entire interest in working with ESCs at Astellas was to use these cells, which can turn into virtually every cell type in the body, to make therapies to treat a wide range of diseases. Tr. 1-95:6-21. Specific to HB-MSCs, Dr. Lanza testified that by the time Dr. Kimbrel successfully made HB-MSCs, around the end of 2009, he was aware MSCs from other sources were in clinical trials for MS and autoimmune diseases, making these "key targets." Tr. 1-105:11-23. There is no dispute this date—around the end of 2009—predates the first meeting with Drs. Wang and Xu (in summer 2010 (Tr. 6-38:24-39:6, 6-39:10-24, 10-29:21-31:4)).

3. While Dr. Kimbrel started her work using Dr. Lanza's previously published method to make HBs, she had to change that method to efficiently make MSCs. Dr. Kimbrel realized early on that the prior method made HBs that were skewed towards becoming red blood cells—which she did not want. Tr. 2-13:14-23, 24:2-26:13; TX-36 at AIRM281691, -694. Despite being told that she wouldn't be able to make HBs without using a particular cytokine called erythropoietin or EPO, Dr. Kimbrel removed EPO from the method and showed that she not only got HBs but those HBs were also not skewed towards red blood cells. *Id.* Dr. Kimbrel then further refined the method.

4. By January 2010, Dr. Kimbrel was confident she had made MSCs. Tr. 2-31:8-11, 2-23:15-20, 2-30:18-31:7. In a May 2010 Progress Report, she reported making MSCs with "95% efficiency." Tr. 2-35:3-36:24; TX-IA at AIRM281778. The same report showed that she made 17 million MSCs using her HB-MSC method, while the direct plating method only produced 4

million. *Id.* While this difference was only four-fold at that time, she later achieved up to twenty-fold more cells from her HB-MSC method. *Id.*; Tr. 2-48:2-20; TX-22 at IMSTEM-1634 (reporting 85 million HB-MSCs compared to 4 million direct plated MSCs).

5. There is no dispute Dr. Kimbrel performed all this work before meeting or hearing about Drs. Wang or Xu. Tr. 2-31:16-18, 2-34:9-17. Nor could there be any serious dispute, for her work is memorialized in numerous contemporaneous documents, including laboratory notebooks, lab meeting presentations, and scientific progress reports. Tr. 2:23:1-36:24; TX-36, TX-45a, TX-44, TX-IA. While Defendants quibble with Dr. Kimbrel's use of the term "MSC-like" (*see e.g.*, Tr. 6-42:10-25), they never dispute that Dr. Kimbrel ***had*** actually made MSCs at this point. To top it off, Defendants called Astellas' cells "MSCs" repeatedly in their internal documents, patent applications, business plans, and grant applications, and should not be heard to assert otherwise now. *See e.g.*, Tr. 6-156:8-12; TX-CC at AIRM14757.

B. The Collaboration Was To Verify The Activity Of Astellas' HB-MSCs

6. At the time of the collaboration, Astellas—then ACT and SCRMI—had a regular practice of collaborating with academics to test its inventive cells in various animal models. Tr. 1-91:12-15, 2-38:20-39:4. Astellas would typically reach out to academics who already had a particular animal model up and running in their lab to verify its cells worked in that model. Tr. 1-91:12-95:5, 1-105:25-106:17, 2-38:20-39:4, 2-39:24-40:4. In such collaborations, Astellas offered the reward of a scientific publication, which is critical to academics in getting promoted, getting grants, and getting tenured. Tr. 1-93:11-21, 3-95:19-96:18. Thus the saying, "publish or perish."

7. Dr. Fortier explained, without any expert rebuttal, that collaborations are common and, where the collaborators perform confirmatory animal or other tests, the company, not the collaborators, gets the intellectual property. Tr. 3-52:3-23, 3-95:19-96:18. In its work on HBs before the collaboration, for example, Astellas collaborated with researchers at Memorial Sloan

Kettering and the University of Florida. Tr. 1-96:18-99:11. While those researchers were co-authors on the 2007 *Nature Methods* article describing Astellas' HBs and HB method, they are not inventors on Astellas' HB patent, and have never claimed to be. *Id.*; TX-6; TX-41. As Dr. Wang admitted, this practice is "common." Tr. 6-154:17-155:3. Indeed, Defendants' T-MSC paper lists Drs. Wang and Xu and five other authors, including one (Adam Lazorchak) who "conceived and designed the research" and "performed the experiments." TX-64 at AIRM171208, -218; Tr. 10-155:23-156:7. Yet only Drs. Wang and Xu are inventors on the T-MSC patent. TX- GB.

8. Similarly, with respect to the work on HB-MSCs, Astellas collaborated with teams from UCLA and the University of Florida, in addition to the Defendants. Tr. 1-105:11-106:24. Data from these collaborations is also included in the '956 patent, but none of them has stolen Astellas' ideas or claimed to be an inventor. This is also consistent with Dr. Fortier's analysis and experience in academic-industry collaborations. Tr. 3-52:3-23, 3-95:19-96:18.

9. Astellas expected its collaboration with Drs. Wang and Xu, then at UConn, would function the same way. Tr. 1-107:8-16, 2-38:20-39:4. Astellas became aware of Drs. Xu and Wang because its scientist, Dr. Lu, was friends with Dr. Xu. Tr. 1-106:25-107:7, 2-37:16-38:8. In July 2010, Astellas entered into an academic collaboration with them to verify that Astellas' HB-MSCs worked in the EAE animal model of MS. *See* TX-16. The parties understood that the end result of the collaboration would be a joint paper, which is exactly what happened. TX-IB at AIRM16052; TX-27; Tr. 10-221:20-222:5, 1-208:19-209:18, 2-57:8-59:6; *see infra* ¶ 53.

C. Defendants' Alleged Contributions To Astellas' Patents Were Minor, Known In The Field And/Or Communicated After Astellas Had Already Conceived Them

1. Using HB-MSCs To Treat MS

10. The idea of using MSCs to treat MS was already well-known, including to Drs. Lanza and Kimbrel. As Dr. Fortier explained, and Defendants admitted, the scientific literature

prior to the collaboration reported numerous studies showing that MSCs were effective in both the EAE animal model and in patients to treat MS. Dr. Fortier walked through five papers published before 2009 reporting that MSCs from various sources had performed well in the EAE model. Tr. 3-28:6-39:15; TX-60; TX-HU; TX-HE; TX-HJ; TX-58. Similarly, Dr. Fortier walked through another five articles showing MSCs had promise in clinical trials for MS before 2009. Tr. 3-41:2-44:12; TX-HL; TX-HM; TX-HI; TX-HS; TX-HK. Dr. Fortier also explained that there was no reason to believe hESC derived MSCs would behave differently since prior literature reported that hESC derived MSCs showed similar results to MSCs from other sources, such as bone marrow. Tr. 3-47:4-48:12; TX-59; TX-GR; TX-HT. Dr. Fortier's expert testimony stands unrebutted, as Defendants' expert, Dr. Bunnell, failed to perform literature searches or even consider whether trials using MSCs to treat MS were ongoing in 2010. Tr. 7-108:23-109:7.

11. And, at least prior to this trial, Defendants said ***the exact same thing.*** They told the Patent Office that "[i]mportantly, MSCs have been found efficacious in the treatment of mice with experimental autoimmune encephalomyelitis (EAE), a well-recognized animal model of MS [citations omitted], as well as MS patients in clinical trials [citations omitted]." TX-A at 2:26-39. And they made virtually identical comments in their 2013 grant application (TX-AV at IMSTEM-18370) and in the *Stem Cell Reports* article (TX-9 at AIRM289980). It is further consistent with Dr. Wang's admission at the outset of the collaboration that "[b]oth mouse and human MSC have been used to ameliorate EAE" (TX-11 at IMSTEM-1525), Defendants' admission in their 2013 book chapter that a 2004 publication taught that "it may be possible in the future to use MSCs to treat multiple autoimmune diseases such as MS" (TX-FD at AIRM297947); and Dr. Wang's admission in his April 2011 presentation that "[u]sing hESC-MSC to treat autoimmune disease" had been "[p]roven to be effective by clinical data using BM-MSC" (TX-X at pdf p. 46).

12. At trial, Defendants tried to walk back or recharacterize these admissions, going so far as to accuse Dr. Fortier of misleading the Court when she testified, based on her review of the literature and materials in this case, that "MSCs Performed Well in EAE Model Before 2009" and "MSCs Showed Promise in MS Clinical Trials Before 2009." Tr. 6-148:7-24. Faced with his admission in the '551 patent—and that he cited several of the same articles in his patent that Dr. Fortier relied on—Dr. Wang first tried to explain it away by saying what he told the Patent Office was wrong, then backtracked to admit some of the papers showed efficacy, then tried to blame his patent prosecution lawyer, Susie Cheng, for writing an inaccurate sentence, even though the same sentence also appeared in Defendants' 2013 grant application, which Dr. Wang—not the patent lawyer—wrote. Tr. 6-148:25-152:18; *see* TX-AV at IMSTEM-18370.

13. Separately, the evidence shows Defendants did not do anything special beyond what was already well-known about how to run the EAE model when using Astellas' HB-MSCs. Dr. Wang admitted that running the EAE model was "easy" in multiple, contemporaneous emails and presentations.[2] TX-16 at IMSTEM-1004; TX-YO at 188:17-24, 242:1-4; TX-15 (Hooke Labs kit "do everything for you"); TX-11 at IMSTEM-1525; TX-X at pdf p. 46. Defendants also told the Patent Office in the '551 patent that they followed the commercial, published protocol when using the kits and running the model. TX-A, '551 patent 53:11-19. And, while Defendants' expert Dr. Bunnell testified that it took his team some time to set up the EAE model in his lab, he admitted that there was "nothing inventive in terms of setting up the EAE model itself." Tr. 7-112:1-5. In fact, Defendants did not, themselves, run the first EAE experiment using Astellas' HB-MSCs. Rather, Dr. Wang took the cells to Yale and someone at Yale performed the experiments. TX-87

[2] Here, too, Dr. Wang tried to rewrite his earlier contemporaneous documents, testifying that "saying it's easy, it's actually not that easy." Tr. 6-44:17-45:2.

at 188:17-24; TX-YQ at 242:1-4.

14. Defendants' whole argument thus hinges on the baseless assertion that it was inventive to suggest using Astellas' HB-MSCs for the same purpose as prior MSCs of all types.

15. But even if Defendants' suggestion ***was*** inventive, Dr. Lanza conceived of using HB-MSCs to treat autoimmune diseases, including MS, in 2009 (*supra* ¶¶ 1-5), long before Defendants' claim to have come up with the concept (TX-FB at 6-7). So if anyone here "invented" the concept, it was Dr. Lanza, not Defendants.

2. Screening For Low IL-6

16. In March 2019, nearly a year-and-a-half into this case, Drs. Wang and Xu admitted in a sworn interrogatory response—signed by their counsel—that the idea of screening HB-MSCs for low IL-6 secretion is "not [an] independently inventive feature[]." TX-V at 8, 18; TX-GQ at 7, 15; Tr. 3-75:3-76:3. Dr. Wang admitted he only added his claim to have "invented" this feature as a litigation tactic, after he had been "push[ed . . .] to the corners" in the litigation and, thus, had "no choice but just to add more claims." Tr. 6-265:18-266:2. Then, under the pressure of cross-examination, he made the preposterous excuse that he didn't list screening for low IL-6 as an invention because "they didn't have time to review the claims" in a year and a half of litigation because they were too busy with T-MSCs, which, in addition to being farcical (the claims are a sentence each), contradicted his earlier testimony that the litigation was all-consuming. Tr. 6-153:12-21, 6-180:20-23, 6-277:14-17.

17. Defendants were correct in their original interrogatory answer. First, as Dr. Xu agreed, the amount of IL-6 a cell secretes is an inherent property of that cell and "[y]ou don't have to do anything" to the MSCs to make them secrete low levels. Instead, all you have to do is test the level the cells secrete. Tr. 10-162:25-163:5, 10-164:2-12. Second, as Dr. Fortier testified, IL-6 was a well-known immunomodulating agent secreted by MSCs, and IL-6 levels were commonly

measured. Tr. 3-70:7-14, 3-71:1-73:18; TX-HF; TX-HO; TX-HN; TX-61. Even the link between IL-6 levels and EAE and MS had been published years before Defendants allege to have come up with this idea. Tr. 3-73:23-75:2; TX-HR; TX-HW; TX-HH. For example, the fact that "blocking IL-6 function can be an effective means to prevent EAE" was published in 1998, and that "[e]levated levels of IL-6 have been noted in autoimmune diseases such as rheumatoid arthritis and MS" and "IL-6 may play a crucial role in the induction phase of EAE" were published in 2002. TX-HR at AIRM299573; TX-HW at AIRM299631; TX-HH at AIRM299438-39. Again, Dr. Fortier's expert testimony stands unrebutted, as Defendants' expert, Dr. Bunnell, was not aware of the significant body of literature showing that IL-6 contributes to inflammation associated with EAE and MS at the time he did his analysis. Tr. 7-122:10-19.

18. Moreover, in their pre-litigation $1.13 million grant application (which Dr. Xu signed, certifying to the State of Connecticut that its contents were "true, complete and accurate" and recognizing that "any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties"), Defendants admitted that, based on the literature, IL-6 "has become *a promising therapeutic target* for treatment of MS." TX-AV at IMSTEM-18383 (emphasis in original). While Dr. Wang initially testified at trial that IL-6 was ***not*** a known therapeutic target for MS, he relented when confronted with the sworn contents of Defendants' grant application. Tr. 6-223:3-5, 6-226:15-227:7.

19. In any event, Dr. Kimbrel discovered that Astellas' HB-MSCs secreted less IL-6 and recognized why it might be important before Defendants began their IL-6 experiments and told Astellas about their work. Tr. 3-76:11-77:3, 3-80:18-21; TX-87 at 362:2-11; TX-HY; TX-HZ; TX-43; TX-62; TX-63. Specifically, it is undisputed that Dr. Kimbrel performed her experiments in March 2012 (Tr. 2-73:15-75:2, 3-77:4-78:17), before Defendants' first tests involving IL-6 in

June 2012, communicated in November 2012. TX-FB at 9; TX-87 at 362:2-11; Tr. 6-222:8-13. As Dr. Kimbrel explained, after reading the literature on MSCs' secretions, she selected IL-6 as one of twenty factors known to be secreted by MSCs to include on a custom antibody array she could use to investigate her HB-MSCs. Tr. 2-72:4-76:1; TX-HY; TX-43; TX-62. She ran experiments in March 2012 and her March 28, 2012 presentation of that data corroborates her observation that HB-MSCs produced much lower levels of IL-6 than found in BM-MSCs. Tr. 2-74:22-75:2; TX-43 at AIRM51823. Dr. Kimbrel recognized the comparatively low IL-6 secretion of Astellas' HB-MSCs, as a combination with other factors, "may be the key to in vivo potency or efficacy" of those cells in an August 7, 2012 email to her Astellas colleague, Dr. McCabe. TX-NI at AIRM21061. In fact, she wrote that such a finding "may allow us to distinguish between functional and non-functional MSCs," and "would be the Holy Grail, useful as QC measure, great for intellectual property and patent protection." *Id.*

20. It is undisputed that Dr. Kimbrel sent this email ***before*** Defendants first told her about their work on IL-6 in November 2012. Tr. 6-222:14-16. While Defendants quibble that Dr. Kimbrel later stated that she only had "a little bit of data on IL-6" and "hadn't followed up on it" (TX-RP), that proves Astellas' point. She ***did*** already have IL-6 data and hadn't followed up on it because she had what she needed. Tr. 2-78:15-25. Simply put, even if measuring the inherent level of IL-6 secretion from HB-MSCs was inventive (it is not), Astellas "invented" it first.

3. Mitotically Inactivating HB-MSCs

21. Dr. Fortier testified that, based on the literature, a scientist would have a "very, very good idea" that mitotically inactivated MSCs would work. Tr. 3-63:23-64:8. She explained that it has long been known that a main way MSCs exert immunomodulatory effects is by secreting cytokines or growth factors (also called "trophic factors") that act on other cells. Tr. 3-56:20-58:25; TX-31. MSCs secrete these factors irrespective of whether they have been mitotically inactivated.

Id. Dr. Fortier discussed five articles, published prior to 2009, showing that mitotically inactivated (irradiated) MSCs maintained their immunomodulatory effects. Tr. 3-60:8-63:11. TX-GS at AIRM259955, -957; TX-HA at AIRM298556, -559; TX-HX at AIRM299638, -640; TX-HC at AIRM298595, -597; TX-GY at AIRM298304.[3] Dr. Fortier further discussed a paper, submitted in 2010, which showed that mitotically inactivated MSCs derived from hESCs kept their immunomodulatory properties. Tr. 3-63:12-22; TX-HT at AIRM299588. Even Dr. Xu agreed that scientists tested irradiated MSCs to see if they still had immunomodulatory effects and published that work before Defendants began their work with Astellas' HB-MSCs. TX-88 at 288:20-289:03. Dr. Fortier's expert testimony is, again, unrebutted, as Dr. Bunnell did not know and did not investigate whether MSCs had been mitotically inactivated prior to 2010. Tr. 7-125:10-126:2.

22. Similarly, the motivation for mitotically inactivating ESC-derived cells—avoiding tumors (TX-88 at 306:8-23)—was known long before Defendants began their work. Tr. 3-53:4-56:19; TX-GZ; TX-HG; TX-HB. Even Defendants' expert, Dr. Bunnell, testified he was "pretty sure the regulatory bodies are going to make [someone] do this lethal irradiation, so that I know that things are safe" because of the risk that "some of those embryonic stem cells could form a teratoma." Tr. 7-64:10-20. He further admitted a skilled artisan at the time could determine the radiation dose to inactivate the cells and still keep their ability to secrete trophic factors. Tr. 7-130:2-22.

23. Consistent with Dr. Fortier's analysis and Dr. Bunnell's admissions, Defendants admitted in sworn interrogatory responses that mitotic inactivation, and specifically irradiation, is not an "independently inventive feature[]." TX-V at 8; TX-GQ at 7. Defendants' pre-litigation

[3] In fact, Defendants cited many of the same articles Dr. Fortier relied on in a pre-litigation 2012 grant proposal where they admitted that it was known that irradiated MSCs maintained their immunomodulatory effect by inhibiting T cell proliferation. TX-51 at IMSTEM-40214, -217.

book chapter admits that, because a major way MSCs work is by secreting factors, MSCs should work even if mitotically inactivated. Defendants stated that "one of the major mechanisms for the MSC activities is their capability of cytokine secretion rather than tissue regeneration. ***Thus, it is possible*** to mitotically inactivate MSCs differentiated from human ES cells and use them for clinical trials to avoid the possible tumorigenicity by residual undifferentiated human ES cells." TX-FD at AIRM297947. Dr. Wang tried to rewrite his admission and redefine "thus" (Tr. 6-169:14-21), but such litigation-inspired rephrasing cannot escape the plain meaning of his own words, much less satisfy the corroboration requirement for interested inventor testimony. Mitotic inactivation was well-known and skilled artisans would have expected it to work with HB-MSCs.

4. Comparing HB-MSCs To BM-MSCs

24. There is no dispute that comparing a new type of MSC (here, HB-MSCs) to a well-known type of MSC (here, BM-MSCs) was a standard, necessary step any scientist would have done. Dr. Fortier explained that BM-MSCs were a common benchmark for newly derived MSCs, citing several articles published before 2009. Tr. 3-84:22-86:14; TX-HV at AIRM299621; TX-GR at AIRM171102; TX-HP at AIRM299564. Defendants' expert, Dr. Bunnell, agreed, testifying ***on direct***, a scientist would "have to, and [that scientist] should want to, compare it to a known mesenchymal stem cell" with "the most widely investigated use at the time was one from bone marrow, so a B-MSC." Tr. 7-72:3-73:6. Dr. Bunnell even went further, stating "the only way to make sound, scientific comparisons, in my opinion is to compare that to – I'll use the term 'gold standard,' . . . a B-MSC is the gold standard." *Id.* Defendants' book chapter admits the same—that hESC-derived MSCs had been reported to "have even stronger immunosuppressive activity than the BM-derived MSCs, according to a recent report (Yen et al. 2009)." TX-FD at AIRM297947. Dr. Xu agreed this meant "it was known in the art, to compare BM-MSCs with ES-MSCs" (Tr. 10-149:4-7), and admitted at his deposition that comparing newly derived MSCs with BM-MSCs

is "very common" and is "what a scientist would naturally do in the situation" (TX-88 at 86:1-9).

D. Defendants' Alleged Contributions To The '551 Patent Were Minor Variations Already Known In The Art

1. Astellas' HB-MSC Method Is The Significant Invention In The '551 Patent

25. The '551 patent claims a method of generating MSCs from hESCs via an HB intermediate and the HB-MSCs created by that method. TX-A at AIRM2903410. As this Court held on summary judgment, "Drs. Kimbrel and Lanza provided [Drs. Wang and Xu] with the protocol to generate HB-MSCs," a point that Defendants did not contest. Dkt. 163 at 7-9. This Court also found that Defendants "have no factual basis to dispute" that Drs. Kimbrel and Lanza "made a significant contribution to the invention." *Id.* at 8. The Court thus found that Drs. Kimbrel and Lanza are at least co-inventors to the '551 patent. *Id.* at 9.

26. As Dr. Brivanlou testified, the '551 patent indicates that the significant invention described in the patent is Astellas' HB-MSC method and the resulting cells—not anything Defendants allege to have contributed. First, the Title of the '551 patent does not mention any of Defendants' alleged contributions. TX-A. The Introduction states that the "present invention relates to a method of generating mesenchymal stem cells from human embryonic stem cells using a multi-step method." TX-A at 1:20-30. This multi-step method involves culturing hESCs, then differentiating the hESCs into EBs, differentiating the EBs into HBs ("hemangio-colony forming cells"), and differentiating the HBs into MSCs, all of which were invented by Astellas, not Defendants. *Id.* As Dr. Brivanlou explained, the description of the invention in the Introduction does not specify that 1) the disclosed method must use a GSK3 inhibitor in a particular amount, 2) the hESCs must be cultured feeder-free, or 3) the hESCs must be cultured in serum-free media. *Id.*; Tr. 4-62:11-16.

27. Similarly, the Background section of the '551 patent describes how Astellas'

invention solves the problem with prior methods. TX-A at 2:63-3:5. This Background section does not relate the benefits of the claimed invention (an "unlimited, safe, and consistent supply of stem cells to be used to treat and prevent autoimmune diseases") to Defendants' alleged contributions. *See id.*; Tr. 4-63:19-23. Instead, as Dr. Brivanlou explained, the benefits are attributed to Astellas' method—deriving MSCs from hESCs via an HB intermediate. Tr. 4-63:24-64:6.

28. As Dr. Brivanlou explained, the "Summary of the Invention" in the '551 patent describes Astellas' invention. It states that the "invention is based on the ***surprising discovery*** that a portion of the HB-containing cells derived from embryonic stem cells (hES), can also differentiate into MSC, designated 'hES-MSC', with high efficiency and consistency." TX-A at 3:13-46 (emphasis added); *see also id.* at 2:65 (defining "HB" as "hemangioblast"); Tr. 4-64:7-15. Neither this initial summary of the invention nor the entire Summary of the Invention, which spans almost five columns, mentions 1) use of a GSK3 inhibitor in a particular amount, or 2) culturing hESCs feeder-free. *See* TX-A at 3:13-8:3. It contains a single embodiment in which serum-free culture of hESCs (using knockout serum replacement or KOSR) is one option, while use of serum is another. *See* TX-A at 3:47-67, 4:14-17.

29. As described by Dr. Brivanlou, the four mentions of a GSK3 inhibitor in the '551 patent's 67 columns of text[4] indicate its use is optional, and not critical. Tr. 4-64:16-65:10, 4-65:23-67:5. The '551 patent states hESCs "may be cultured ***in any way known in the art***, such as in the presence or absence of feeder cells" and continues that the GSK3 inhibitor BIO "can increase the embryoid body formation and subsequent hemangioblast forming efficiency," indicating such use is optional. TX-A at 13:47-54. The "Materials and Methods" of Example 1 expressly states hESCs may be cultured "with or without adding of 0.05-0.2 μM of BIO," again indicating such

[4] The last two mentions of a GSK3i are in claims 1 and 11. TX-A at 67:16-68:11, 68:37-38.

use is optional. TX-A at 51:1-14. The last two mentions of use of a GSK3 inhibitor in the text simply describe data in Figures 28, 29, and 30. TX-A at 10:28-37, 52:9-18. These figures do not concern the effects of GSK3 inhibitor treatment of hESCs on MSCs. TX-A at 10:28-37; Tr. 4-67:6-68:8. Rather, they only show data for effects "on the differentiation of embryoid bodies (EB) from hES cells" (Fig. 28), on "EB formation numbers" (Fig. 29), or "hemangioblast forming efficiency" (Fig. 30). *Id.* As Dr. Brivanlou explained, addressed further below, these figures and descriptions show Defendants used the GSK3 inhibitor for precisely the same purpose and with the same effect as described in Dr. Brivanlou's 2004, 2006, and 2009 publications.

30. The timeline of events in the '551 patent's prosecution history likewise indicates that none of Drs. Wang and/or Xu's alleged contributions are significant to the claimed invention. First, the original claims expressly made use of a GSK3 inhibitor ***optional***, for the first step recited "culturing human embryonic stem cells with serum free media ***with or without GSK3 inhibitors.***" TX-8 at AIRM293646; Tr. 4-68:17-69:1, 8-174:22-175:4. Defendants only amended the claims to require the GSK3 inhibitor in response to the Examiner's rejection of those claims as "anticipated by," or claiming the same invention as, Astellas' HB-MSC PCT publication. TX-8 at AIRM295651-52, -654 ("Lanza teaches the same method steps to produce the same cells."); *id*. at AIRM295774-98. Defendants filed this amendment on January 17, 2017 and, despite also submitting a sworn declaration attesting they had possession of the invention before Astellas' patent filing (*i.e.,* reciting only an optional GSK3 inhibitor), they did not disclose to the Patent Office that they got this information ***from Astellas***. *Id.*; Tr. 8-171:19-173:2.

31. Second, neither provisional applications to which the '551 patent claims priority (*i.e.,* TX-3 and TX-5) discusses using a GSK3 inhibitor or BIO. Tr. 4-70:19-71:8, 6-193:4-8. In fact, Defendants referred to the first provisional application as designed to "prevent [Astellas] from

using ***their*** technology to go to clinic and develop product" (TX-Z at IMSTEM-31515), as an "***attack patent***" (TX-AA at IMSTEM-27835), and as one they could use to "***ask for royalty*** from [Astellas] if they have successfully marketing ***their*** product" (TX-14 at IMSTEM-9108). While Defendants' counsel tried to dismiss these pre-litigation emails as "homespun" efforts by "inexperienced business people" that were merely "loose talk" and "intemperately worded" (Tr. 11-66:9-10, 1-65:4-11, 1-71:11-13, 11-65:14-16), Dr. Wang testified he meant exactly what he wrote. Specifically, Dr. Wang explained his use of "attack patent" meant "[i]t will be used for – as a bargaining chip to – for any future litigation" and that "we cannot use this [patent] for real product development, but only for future litigation use. If anybody sue me, then we can use that as a counterattack, so – to exchange for some kind of licensing exchange and the patent exchange." Tr. 6-138:19-139:20. In short, from the outset Dr. Wang intentionally filed a patent covering Astellas' technology with the plan to attack Astellas with it in future litigation. He did not file it in an attempt to protect some alleged improvement involving a GSK3 inhibitor, as Defendants now assert.

2. Use of a GSK3 Inhibitor (Specifically BIO) at 0.05-.2 uM Concentration In Serum-Free And Feeder Free Medium Was Not A Significant Contribution

32. Defendants initially alleged that Drs. Wang and Xu contributed to the first step—and only that step—of the method of making HB-MSCs recited in claim 1 of the '551 patent, the only independent claim. TX-V at 5-6; TX-GQ at 5-6. Defendants also alleged they contributed the specific GSK3 inhibitor, BIO, to dependent claim 11. TX-V at 8; TX-GQ at 7-8. Defendants also admitted that Dr. Kimbrel carried out the remaining four steps in claim 1 of the '551 patent prior to Defendants' alleged invention. TX-V at 5; TX-GQ at 5; *see also* Dkt. 163 at 3.

33. As to the remaining claims of the '551 patent, Defendants, in sworn interrogatory responses in March 2019, admitted "[t]he remaining dependent claims recite additional useful, but not independently inventive features." TX-V at 8; TX-GQ at 7-8. These dependent claims (and

more features in claim 1) include limitations regarding low IL-6 secretion (claims 1 & 2) and mitotic inactivation (irradiation) (claims 6 & 7)—two features Defendants' later in this litigation asserted were inventive concepts they contributed to Astellas' patents.[5] Dkt. 91 at ¶¶ 26-27, 33. While Defendants tried to reverse these admissions in "amended" interrogatory responses served after Astellas' opening expert reports (TX-FB at 9-12) and at trial (Tr. 6-276:5-277:13), Dr. Wang testified that Defendants' reason for changing course was purely to gain leverage in the litigation. Tr. 6-265:18-266:2 ("I think this case can be settled and can be resolved, but actually you guys are trying to push us to the corners, and ***we have no choice but just to add more claims***.").

34. Thus, Defendants originally alleged Drs. Wang and Xu contributed four things to the claims of the '551 patent: "(1) culturing real (not MA-09) hESCs, (2) doing so in a serum-free media, (3) doing so in the absence of feeder cells, and (4) doing so in the presence of inhibitors of GSK3, at 0.1 [sic[6]] to 0.2 µM," and the GSK3 inhibitor called "BIO" or (2'Z,3'E)-6-Bromoindirubin-3'oxime (dependent claim 11). TX-V at 5-6 & 8; TX-GQ at 5-6 & 8. During trial, Defendants dropped their allegation regarding MA-09 cells not being "real" hESCs (Tr. 4-5:21-9:1), leaving only three, all of which were known prior to Defendants' alleged conception of them.

35. The parties do not dispute that two of the allegations—serum-free and feeder-free culture of hESCs—were both known and "routine" by the mid-2000s, before the collaboration began. Tr. 10-172:19-21. Both Dr. Lanza's and Dr. Thomson's group (where Dr. Xu trained) published reports of serum- and feeder-free cultures in 2005 and 2006, respectively. Tr. 1-129:18-130:11; TX-GP; Tr. 10-175:2-177:3 (use of mTeSR1 for serum-free and feeder-free hESC culture "routine"); TX-YG; TX-YH. Consistently, Dr. Kimbrel explained that Astellas cultured hESCs

[5] For the reasons discussed *supra* and *infra* with respect to Astellas' '321 and '956 patents and the '551 patent, these contributions are not a basis for Drs. Wang and/or Xu to be co-inventors.
[6] Claim 1 recites "a concentration ranging from ***0.05µM*** to 0.2 µM." TX-A at claim 1.

under feeder-free conditions, and her decision to use feeders was "more of a business decision." Tr. 2-83:3-15; *see also* TX-IA at AIRM281787 (SCRMI scientist reporting work with a "culture system [that] uses feeder free conditions"); TX-EV at AIRM13416 (reporting "Benefits of Micro-Carriers" include "No MEF – Serum free chemically defined media allows for acceptability for clinical trials" and "Greatly enhanced Hemangioblast differentiation efficiency vs 2D feeder free culture system"). Dr. Brivanlou explained why such business decisions would be made: it is more expensive to culture hESCs serum-free and feeder-free, so early (exploratory, non-commercial) work often uses feeder cells and serum for cost reasons. Tr. 4-37:1-8.

36. The parties dispute the purpose for which a GSK3 inhibitor is used in the first step of the '551 patent. As the patent itself and the testimony indicate, this purpose is to maintain the hESCs in an undifferentiated state and improve embryoid body formation, which is the exact same purpose Dr. Brivanlou described in his 2004 *Nature Medicine* paper.[7] Tr. 4-49:10-50:19; *compare* TX-7 *with* TX-A. While Dr. Wang and Defendants' expert, Dr. Perry, disagreed at trial (*see, e.g.*, Tr. 6-57:23-58:17, 8-36:18-38:6), the '551 patent itself indicates that the purpose of this first step is to maintain the hESCs before beginning the differentiation process. TX-A at 51:1-16 (describing culture of hESCs with or without BIO, then stating "hESC cells ***were then differentiated*** into EB cells"), Fig. 29; Tr. 4-49:10-50:19.

37. In fact, Dr. Wang's work using a GSK3 inhibitor started with and followed Dr. Brivanlou's teachings in his publications on use of BIO with hESCs. As documented in his laboratory notebook, Dr. Wang started with Dr. Brivanlou's 2 μM concentration of BIO on October 4, 2010. Tr. 6-216:11-17; TX-BT at IMSTEM-42984. After seeing that concentration

[7] Dr. Brivanlou further explained that his experiments in his 2004 *Nature Medicine* paper also involved serum-free and feeder-free culture of hESCs using BIO. Tr. 4-51:14-19.

killed the cells (a risk Dr. Brivanlou warned about in his 2006 publication (TX-34 at 125-26)), Dr. Wang used a lower concentration of BIO, which followed Dr. Brivanlou's instruction that it is "critical to find out a minimal concentration of BIO" to avoid cell death (TX-34 at 125-126). Ten days and three notebook pages after using the higher, 2 µM concentration, Dr. Wang saw his "exciting" results showing that 0.25 µM of BIO worked. Tr. 6-216:11-17; TX-BT at IMSTEM-42987. When Dr. Wang realized during cross-examination how simple this appeared, he tried to backtrack, asserting that "I ordered this BIO actually pretty early" and "maybe [he] did more than" the work in his notebook but failed to "write down all [he] did." Tr. 6-215:12-216:4. Yet, the October 14, 2010 experiment with BIO was the ***only*** experiment he identified on direct as showing his BIO work. *See* Tr. 6-58:22-59:16 (discussing TX-BT at IMSTEM-42987 (notebook page 42)).

38. Ultimately, Dr. Wang merely replicated Dr. Brivanlou's work with BIO, as taught in Dr. Brivanlou's pre-2010 publications. Dr. Brivanlou's earliest paper on BIO disclosed that 1 and 2 uM concentrations of BIO in serum-free and feeder-free media maintained hESCs in an undifferentiated state and had the same effect on increasing the number of EBs made from hESCs. Tr. 6-57:9-22, 6-59:7-16, 4-49:23-50:2. Dr. Wang even credited Dr. Brivanlou's 2004 *Nature Medicine* paper as disclosing "BIO(2µM) has been shown to maintain hESC culture in CM for 5 days(Ali H Brivanlou, Nature Medicine 2004)" in his February 2011 draft presentation. TX-W at slide 20. As Dr. Brivanlou testified, Dr. Wang's work in Figure 29 of the '551 patent replicated Dr. Brivanlou's work in Figure 5 of his 2004 *Nature Medicine* paper. Tr. 4-51:1-19; TX-A, '551 patent Fig. 29, TX-7 at AIRM290001. While Dr. Wang used a lower concentration than Dr. Brivanlou reported in his 2004 paper, that merely followed Dr. Brivanlou's instruction in his 2006 paper to use the lowest effective dose to avoid side effects. Tr. 4-53:10-15; TX-34 at 125-26.

39. Defendants' contemporaneous documents show they did not believe that including

a GSK3 inhibitor at the first step of culturing hESCs was significant or inventive. After Dr. Wang saw his "exciting" results with 0.25 µM of BIO in October 2010, Defendants did not mention it in their: 1) January 2011 grant (TX-CC); 2) September 2011 draft business plan (TX-AK); 3) March 2012 ImStem Business Proposal (TX-19); 4) first, July 2012 "attack" patent application (TX-4); 5) November 2012 Caspase-3 grant progress report (TX-AF); 6) 100-page January 2013 grant application, for which they received $1.13 million; 7) second, February 2013 application for the '551 patent (TX-5); or 8) January 2014 *Stem Cell Reports* article on the work from the collaboration (TX-9). While Defendants mentioned using a GSK3 inhibitor in their June 2013 and January 2015 PCT patent application and amendment, these explicitly stated that use of a GSK3 inhibitor was optional, not required.[8] TX-8 at AIRM293577, -646. While Defendants complained on Dr. Xu's redirect that a GSK3 inhibitor was mentioned in Dr. Wang's April 2011 presentation (Tr. 10-231:22-233:1), they omit that the only discussion of the GSK3 inhibitor, feeder-free or serum-free work was in the section of that presentation on hematopoietic stem cells ("HSC")—not the section on MSCs—as Dr. Xu admitted. Tr. 10-191:21-192:10; TX-X at pdf pp. 3, 14-35. In fact, nearly all the *in vitro* data on MSCs in the MSC section of Dr. Wang's presentation (TX-X at pdf pages 36-49) came from Dr. Kimbrel. *Compare* TX-X pdf p. 40 *with* TX-22 at IMSTEM-1634, Fig. 4; TX-X at pdf p. 41 *with* TX-22 at IMSTEM-1634, Table 1; TX-X at pdf p. 42 *with* TX-GW at IMSTEM-7994 at pdf p. 6; TX-X at pdf p. 43 *with* TX-GW at IMSTEM-7994 at pdf p.7.

40. While Defendants' expert, Dr. Perry, opined (without reviewing relevant testimony or documents) that use of a GSK3 inhibitor at the first step of the method was critical in order to

[8] Dr. Xu attempted to rewrite the statement that the method could be performed "with or without GSK3 inhibitors," stating that "'with' means to test, 'without' means the control. So it is clear the meaning must be–must be with GSK3 inhibitor." Tr. 10-185:4-12. But Defendants' patent expert, Dr. Zerhusen, testified that the "with or without" language means the GSK3 inhibitor is optional and the examiner would have "read that out of the claim." Tr. 8-174:22-175:4.

get any HB-MSC product, his testimony directly contradicted that of Dr. Wang. Tr. 8-34:18-24. Dr. Wang testified that "adding GSK3 doesn't change the functionality of the final product MSCs" and that these final product MSCs "work the same" as those made without use of a GSK3 inhibitor. Tr. 6-199:2-10. Worse, Defendants actively shielded Dr. Perry from relevant evidence, as apparent from Dr. Perry's admission that he "wasn't invited to" and "didn't have access to [Dr. Wang's] testimony" and he even "didn't know it occurred." Tr. 8:57:23-58:6. Dr. Perry's opinion thus is entitled to no weight, as it was completely divorced from the facts and evidence in this case.

3. Contrary To Defendants' Arguments, Astellas' Method Is Highly Efficient And Yields Clinically Relevant Numbers Of Cells

41. Defendants' contemporaneous documents show their litigation-contrived claim—that Astellas' method resulted in poor cell yield—is incorrect. First, Dr. Wang admitted under cross-examination that he had described Astellas' method as "highly efficient." Tr. 6-245:16-247:1. Second, Dr. Wang presented internally Dr. Kimbrel's data showing she obtained 85 million MSCs using her HB-MSC method compared to 4 million MSCs with the older direct plating method. TX-X at pdf p. 41; Tr. 6-204:14-205:6. Dr. Wang's summary slide in this presentation also stated that adding the HB step—not use of a GSK3 inhibitor—increased the yield of MSCs. TX-X pdf p. 48 ("Using HB blast method to generate MSC increase cell number yield and shorten the maturation time").

4. The Patent Examiner Did Not Search For GSK3 Inhibitors

42. Defendants' reliance on the Examiner's Reasons of Allowance to support inventiveness of the GSK3 limitation is entirely misplaced. First, the Examiner ***never*** performed a prior art search targeting GSK3 inhibitors. Tr. 8-189:22-24. Dr. Zerhusen opined that if the GSK3 limitation was important for allowance, the Examiner was supposed to search specifically for art on GSK3 inhibitors. Tr. 8-184:6-21. But the Examiner ***never did so***, as Dr. Zerhusen candidly

admitted. Tr. 8-184:22-185:21, 8-186:23-189:21; TX-40 at AIRM295975-78.

43. Second, even though Defendants disclosed Dr. Brivanlou's 2004 paper to the Patent Office, nothing in the record suggests the Examiner ever had or considered Dr. Brivanlou's 2006 or 2009 publications. Tr. 8-181:20-182:1. If the Examiner had Dr. Brivanlou's 2006 and 2009 publications, he would have seen that Dr. Brivanlou instructed that it was "critical to find out a minimal concentration of BIO" to avoid "any significant effect on [hESCs] viability or growth rate." TX-34 at 125-126. He would also have found the specific concentration range claimed by Defendants—0.05 to 0.2 μM—was within the range Dr. Brivanlou disclosed in his 2009 publication. TX-33. Dr. Zerhusen did not analyze whether the Examiner was actually correct in allowing the '551 claims. Tr. 8-182:10-19. And as the evidence makes clear, he was not, for the Manual of Patent Examining Procedure ("MPEP") instructs examiners that patents are *prima facie* obvious where the prior art discloses overlapping ranges. Tr. 8-183:2-11; MPEP § 2144.05 ("In the case where the claimed ranges overlap or lie inside ranges disclosed by the prior art a prima facie case of obviousness exists."). According to the MPEP, if the Examiner had been made aware of Dr. Brivanlou's 2006 and 2009 publications, he would have rejected the '551 claims as obvious in view of their overlapping GSK3 inhibitor concentrations.

44. Finally, as Dr. Zerhusen confirmed (and contrary to Defendants' allegation in their opening), the Patent Office generally does not analyze inventorship. Tr. 8-168:10-23. And Dr. Zerhusen confirmed there was no indication that the Defendants told the Patent Office anything about the collaboration with Astellas' scientists, Drs. Kimbrel and Lanza. Tr. 8-171:25-172:5.

E. Defendants Competed Unfairly, Harming Astellas

45. Defendants deceived Astellas into continuing to provide HB-MSC cells, data, and know-how as part of the collaboration, constantly assuring Astellas that they would keep this material confidential and only use it for purposes of the collaboration. Tr. 2-52:3-62:5; TX-GW;

TX-39; TX-IB; TX-25; TX-27; TX-GT; Tr. 6-176:4-10, 6-177:10-178:3, 10-60:17-61:23. Yet, they plotted to and used Astellas' confidential, proprietary materials to 1) file patents, 2) solicit businesses and investors in ImStem, 3) seek grants to fund ImStem, and 4) jump-start Defendants' work on T-MSCs. *See, e.g.*, TX-AA; TX-Z; TX-14; TX-26; TX-AK; TX-19; TX-18. Defendants did all this despite understanding that they should have kept Astellas' information confidential. Tr. 6-105:2-18, 10-124:11-15; TX-88 at 68:17-69:2; TX-11; TX-87 at 97:14-98:1.

46. Defendants agreed that, per academic norms, they would keep any information Astellas shared during the collaboration confidential. TX-88 at 68:17-69:2; Tr. 6-173:8-174:24; 10-124:11-15. In addition, Dr. Kimbrel emailed several times seeking—and receiving—reassurances from Drs. Wang and Xu that they would keep Astellas' information confidential and only use it for certain, limited purposes. Tr. 2-52:3-62:5; TX-GW; TX-39; TX-IB; TX-25; TX-27; TX-GT. At trial, Defendants tried to recharacterize their responses to mean something other than what the plain language stated. For example, Defendants contended at trial that Dr. Wang's contemporaneous email stating he would "only use [Dr. Kimbrel's MSC differentiation data into adipocytes and osteocytes] for departmental presentation" (TX-39), actually meant he could use that data for departmental presentations ***and grant proposals*** at any time, including in Defendants' application for a Connecticut-state grant for ImStem in 2013, from which they obtained $1.13 million in funding (Tr. 6-233:4-236:7). Such litigation-inspired recharacterizations cannot, however, overcome the contemporaneous plain meaning of the statements.

1. Defendants Filed Patents On Astellas' Confidential Information

47. Defendants emails reveal their intentional and willful bad acts: describing the first application for the '551 patent as an "attack patent" that would "prevent [Astellas] from using their [own] technology to go to clinic and develop product" and could be used to "ask for royalty from [Astellas] if they have successfully marketing their product." TX-Z, TX-AA, TX-14. While

Defendants' counsel tried to downplay these as "Dr. Wang's loose talk" (Tr. 1-71:11-13) or "Dr. Wang's intemperately worded emails about attack patents and blocking ACT" (Tr. 11-65:14-16), Dr. Wang's ***direct*** testimony—meant to clarify his "intemperate" statements—instead proved he meant exactly what he said. He wanted to attack Astellas, then ACT, with a patent he had no intention of commercializing and use it as a "bargaining chip" for use in "future litigation." Tr. 6-138:19-139:20. That is exactly what "attack" means.[9]

48. Defendants' many attempts to hide Astellas' involvement in the technology they claimed as their own in the '551 patent also reveals their bad faith. First, Defendants concealed Astellas' involvement from UConn in their invention disclosure. When required to "describe any materials obtained from third parties (such as research collaborators or companies, with or without a Material Transfer Agreement) that were used in the development of the invention" Defendants falsely replied "None." TX-14 at IMSTEM-9118. In their internal, cover email discussing this form, Dr. Wang told Dr. Xu it covered the collaboration with Astellas and they wanted to use it to

[9] Defendants' also spent a bewildering amount of time trying to excuse their behavior by arguing the stalled negotiation of a formal material transfer agreement ("MTA") was somehow an attempt by Astellas to strip them of their intellectual property rights, and implied this triggered their patent filing covering Astellas' technology. *See, e.g.,* Tr. 1-179:6-20; 10-41:6-42:6. Defendants' counsel even led Dr. Xu—a non-lawyer with no legal experience—to testify as to how the redlined draft of the agreement should be interpreted. Tr. 10-41:6-42:6. This argument fails for multiple reasons. First, Defendants plotted to form a business around Astellas' technology by September 2011 (TX-AK) ***before*** Astellas sent the draft MTA in January 2012 (TX-UB). Second, Defendants completely mischaracterize the negotiation (in emails that Drs. Xu and Wang were not on). Mr. Vincent stated the reason why ACT could not accept UConn's edits to the MTA was that, as edited, if UConn obtained a patent that might block ACT's commercialization of its own HB-MSCs, "merely the option to negotiate an exclusive license unfortunately may not be enough comfort." TX-XV at AIRM278369. He did not propose to "unfairly extinguish [Defendants'] patent rights." Tr. 11-65:23-25. Third, the unedited part of the draft MTA, which Defendants' counsel argued Defendants had accepted (*see* Tr. 1-170:21-171:6), required Defendants to "promptly disclose [any] Invention to ACT" (TX-XU at IMSTEM-4972). Defendants never told Astellas they filed the application for the '551 patent. Tr. 1-126:21-127:10; 2-65:16-66:10. In any event, there is no dispute that the MTA was never signed, and thus cannot control.

ask for a royalty if Astellas successfully sold a product. TX-14 at IMSTEM-9108. Second, Defendants concealed Astellas' involvement from the Patent Office, never admitting their collaboration with Astellas. Tr. 6-181:25-183:9, 8-171:25-173:2. This is so even though the Examiner rejected their proposed claims as "anticipated by," or claiming the same invention as, Astellas' HB-MSC PCT application. Rather than admitting Astellas' involvement, Defendants filed a sworn statement saying they possessed the invention before Astellas without mentioning that it was ***Astellas*** who provided the method in the first place. *Supra* ¶ 30.

2. Defendants Used Astellas' Confidential Information To Solicit Business And Investors

49. Defendants formed ImStem based on Astellas' HB-MSC technology, not T-MSCs as they alleged at trial. Their September 2011 draft business plan discusses HB-MSCs, and is silent on T-MSCs. TX-AK at AIRM296722-723; Tr. 3-111:21-112:16. The same is true of their March 12, 2012 Business Proposal. TX-19 at IMSTEM-40440, -444-45; Tr. 3-112:20-114:1, 6-245:16-247:1. On April 2, 2012, a mere half hour after receiving an email from Dr. Kimbrel asking them to agree to confidentiality and limited use of Astellas' materials in order to continue to receive such materials (TX-27 at IMSTEM-5467), Dr. Xu asked Dr. Wang for summaries of patents in a document identifying patents from Astellas, which they called one of "two major competitor" (TX-26 at IMSTEM-40416, -419). About four hours after emailing Dr. Wang, Dr. Xu replied to Dr. Kimbrel, stating "We like you suggestions. Let's move on asap." TX-27 at IMSTEM-5466.

50. As Dr. Fortier explained, this behavior "was not even close to within any normal realm" of scientific norms and practices. Tr. 3-115:14-116:10. Notably, Defendants created both of these business plans and performed their search of their "major competitor" Astellas' patents ***before*** Astellas' inclusion of a slide of EAE data—attributed to Dr. Wang and for which Astellas later apologized—at a conference in London in May 2012. TX-XX at IMSTEM-5760, -762; TX-

MV; Tr. 6-250:15-252:10. While Defendants testified they never provided Astellas' HB-MSC technology to ImStem investors (Tr. 6-188:12-18), that is false. Defendants sent at least Dr. Men, an ImStem investor (Tr. 6-188:19-189:6), the March 2012 business proposal (TX-19) and included him on emails attaching their "attack patent" (on Astellas' method) they planned to use to "prevent [Astellas] from using ***their*** technology to go to clinic and develop product" (TX-AA; TX-Z).

3. Defendants Used Astellas' Confidential Information In Grants For ImStem

51. Defendants also unfairly competed by using Astellas' technology to apply for and obtain at least a $1.13 million dollar grant from the state of Connecticut for ImStem. Indicative of their cover-up attempts, Defendants could not keep their story straight here either. In July 2019, they said the grant covered HB-MSCs in interrogatory responses signed under penalty of perjury. TX-MJ at 12-13. A year later, Defendants' counsel told the Court that it covered only T-MSCs, stating "there is no reference in the document to HB-MSCs." Dkt. 221 at ¶ 84. At trial, Dr. Wang testified that his counsel was wrong and the grant discussed HB-MSCs and not T-MSCs. Tr. 6-239:4-16. Then, three days later, Mr. Green contradicted Dr. Wang, testifying the grant was on T-MSCs. Tr. 9-76:4-12. And a day after that Dr. Xu contradicted them both (and his own testimony 30 seconds prior) stating the grant covered ***both*** HB-MSCs and T-MSCs. Tr. 10-202:17-23.

52. There is no dispute Defendants included Astellas' HB-MSC technology—including Dr. Kimbrel's data that Dr. Wang said he would "only use it for departmental presentation" (TX-39 at IMSTEM-2553)—in this $1.13 million dollar grant application. As Dr. Fortier explained, Defendants incorporated data that Dr. Kimbrel sent Dr. Wang on March 28, 2011, into this grant application dated January 4, 2013. Tr. 3-117:12-118:5; TX-GW at IMSTEM-7994; TX-AV at IMSTEM-18366, -376. While Defendants made several attempts at trial to excuse their behavior, claiming variously that Dr. Wang really meant he would use the data for his departmental presentation ***and grants*** despite stating he would use it "only" for the departmental presentation

(Tr. 6-233:4-236:7); that despite Defendants' expert, Mr. Green, saying the grant was for T-MSC work, Dr. Xu corrected his earlier testimony to say he actually used part of it to pay for HB-MSC work (Tr. 10-202:11-203:13); and Dr. Xu's unsupported testimony that he "kind of remember we told Erin [Kimbrel] that we are applying for that grant" (Tr. 10-231:13-19); their litigation-concocted explanations cannot overcome what the contemporaneous documents actually say.

53. Defendants then tried unsuccessfully to cast themselves as victims of a disagreement over authorship of two papers as an excuse for their behavior. Tr. 6-131:6-132:15, 10-80:15-84:6. Defendants omit, however, that many of their intentional bad acts occurred before this issue arose in 2014 (*see* TX-DZ at AIRM38243) and, more importantly, that ***Dr. Xu suggested*** that the parties do exactly what happened, *i.e.*, they "publish [their] own data separately according to different focuses" in the case of disagreement (TX-IB at AIRM16052; Tr. 10-221:20-222:5). Dr. Xu also rejected Astellas' offer to publish two papers, with Drs. Xu and Wang being co-authors on Astellas' methods paper provided some of the EAE data was included, despite first agreeing to it. Tr. 10-214:13-215:11; TX-27 at IMSTEM-5466. While Dr. Xu's angst at not publishing in his journal of choice appeared genuine, Astellas is not the cause of that disappointment. Rather, it is the result of Dr. Xu's own suggested approach and the fact that the reviewers for that journal had other, additional reasons for their rejection, including "concerns about various aspects of the characterization and particularly the degree of mechanistic insight." TX-DZ at AIRM38244. And in the end, Defendants got their side of the bargain—publication in a journal that Defendants told the State of Connecticut, under oath, was "prestigious." TX-AI at IMSTEM-21601.

4. Defendants Jump-Started Their T-MSC Work With Astellas' Information

54. Defendants also unfairly competed by using Astellas' HB-MSC technology to jump start their T-MSC work. Dr. Xu twice testified at his deposition that Defendants used Astellas' HB-MSCs as a shortcut, stating ACT was "generating MSC from ES cells, and so I think that will

give us a shortcut to do the test" and "ACT provided a shortcut for us to test the cells."[10] TX-88 at 75:11-17, 84:22-85:4. As Dr. Fortier explained, Defendants' documents and admissions show they used Astellas' HB-MSC technology as a "shortcut" to jump start their work with T-MSCs. Tr. 3-118:6-123:9; TX-AI; TX-AJ. Defendants admitted so in an August 2016 progress report for their $1.13 million dollar grant, explicitly stating the work with Astellas' HB-MSCs that was "published in the prestigious journal Stem Cell Reports (June, 2014)" was the ***basis*** for their development of "a new stem cell therapy product IMS001," their T-MSCs. TX-AI at IMSTEM-21601. Indeed, Defendants did not have practical experience in deriving MSCs from hESCs prior to the collaboration. Tr. 6-155:4-9, 168:15-18, 3-111:14-114:7, 5-17:21-18:3.

55. When confronted with this evidence, Defendants resorted to their common tactic—to deny what their own, pre-litigation documents say. For example, Dr. Xu affirmed to UConn he "first conceived" the T-MSC invention was on March 1, 2012 (TX-CN at IMSTEM-18171; *id.* at -173 (signing to confirm "the completeness and accuracy of the information in this disclosure")), which is years after Drs. Xu and Wang first accessed Astellas' HB-MSC technology in August 2010. Faced with that admission, Dr. Xu said the invention disclosure form he signed on June 6, 2012 cannot be used "as the exact time because our memory is way before that." Tr. 10-206:11-23. He further claimed the March 2012 date he told UConn was only an "estimate" and that the "real conceiving time is much earlier," without pointing to any corroborating documentary evidence.[11] *Id.* And Dr. Xu's explanation, that he estimated specific dates (not just months, but

[10] Dr. Xu tried to take back this statement at trial, stating that he only meant that the "shortcut" involved getting the permit to do animal testing at UConn in the first instance. Tr. 10-58:24-59:14. Dr. Xu's deposition testimony, however, clearly states that the use of Astellas' HB-MSCs are what gave the shortcut and says absolutely nothing about animal permits.

[11] Defendants' reference to Dr. Xu's work with trophoblasts and related documents using that term while working under Dr. Thomson from 1990-2005 (*see* Tr. 10-14:10-16:22, 10-226:22-25) is an irrelevant sideshow. Even Dr. Xu did not suggest that he developed T-MSCs in that time frame.

specific dates) for conceiving and recording his invention of T-MSCs three months earlier than his submission when instead it was years earlier is outlandish; it is akin to estimating that you last went on vacation on "August 12, 2020," then claiming it was actually in 2018.

56. And even after they began focusing on T-MSCs, they falsely presented data generated using Astellas' MA09-derived HB-MSCs as T-MSC data in their FDA submissions, to the state of Connecticut, and to the scientific community. Seeking IND approval of their T-MSC product IMS001, Dr. Wang passed off MA09-derived HB-MSC data from Figure 4B of the joint paper as T-MSC data in Figure 9 of Defendants' FDA submission. Tr. 6-270:3-271:22; TX-UI at IMSTEM-22947; TX-9 at AIRM289987. Both Drs. Wang and Xu admitted they used HB-MSC data in Figure 9. Tr. 6-271:16-22, 10-46:18-22. Dr. Xu tried to blame an unnamed former employee for pulling the wrong data (Tr. 10-47:3-9), but Dr. Wang admitted that "***I*** maybe used the wrong datas" (Tr. 6-271:16-22). Dr. Xu also tried to excuse the error by claiming the data was later removed. Tr. 10-46:23-47:2. This claim, too, is baseless, for Defendants provided no evidence of any correction submitted to the FDA and Dr. Xu admitted they never informed the FDA the data was false. Tr. 10-119:6-20. Further, in a Connecticut grant submitted under oath, Dr. Wang falsely labeled MA09-MSC data from Figure 4A of the joint paper as T-MSC data to show purported "stronger immunosuppressive efficacy" of T-MSC. Tr. 6-270:23-274:3; TX-UO at IMSTEM-24199, Fig. 4A; TX-9 at AIRM289987. In a poster presentation relied on by Mr. Green for superiority of T-MSCs, Dr. Wang passed off the same MA09-MSC data as T-MSC data. Tr. 6-268:1-270:2; TX-UH; TX-9 at AIRM289987.

57. Dr. Wang admitted that Figure 4A "was always HB-MSC data in our paper." Tr. 6-

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To suggest that he did would completely contradict Defendants' patent application filing on such cells ***a decade later*** in 2012. *See* TX-GB (first provisional applications filed July 11, 2012).

269:5-20. He knew labeling it as T-MSC was false as he immediately admitted it when confronted with that data, before being shown the joint paper. Tr. 6-268:22-269:4. This would be impossible unless he knew the data was false in the first place. Dr. Xu tried to cover this falsehood by arguing Defendants submitted the false data in Figure 4A to *Stem Cell Reports*, not FDA, despite Dr. Wang's admission and the rigorous, months-long effort involved in such a peer-reviewed publication. Tr. 10-46:1-7, 10-113:16-114:3. He testified, agreeing with a leading question from his counsel, that Defendants corrected their error after Dr. Wang's testimony and "put in the HB-MSC data in the article, the joint article so that's correct." Tr. 10-46:14-17. When confronted with the lack of any documents proving this allegation, Dr. Xu testified that he saw them but didn't give them to the Court because "the exhibits are supposed to be provided in a certain time."[12] Tr. 10-116:18-117:13. Defendants' counsel then tried to suggest that there was evidentiary support for this proposition in his closing, referring to an email with *Stem Cell Reports*. Tr. 11-68:13-21. But that email—added to the record at Astellas' request—proves Defendants' allegations are false. It does not "put in the HB-MSC data in the article," as Defendants' counsel led Dr. Xu to testify. Rather, it shows that the day after he testified, Dr. Wang emailed *Stem Cell Reports* stating a "[r]ecent ***internal data review*** found a mistake in figure 4A" and asked how to submit an erratum. TX-YU at IMSTEM-46493. Setting aside that this statement, too, is false—it was cross-examination, not an "internal data review," that uncovered Dr. Wang's falsehood—Dr. Wang did not submit any HB-MSC data as Dr. Xu testified. *Id*. at IMSTEM-46492, 494.

58. In any event, Dr. Wang admitted at least one purpose for including the HB-MSC data was to show T-MSCs "work all the same" as Astellas' cells. Tr. 6-274:19-275:8. Defendants

[12] Dr. Xu's excuse that it was too late to proffer new evidence was belied by Defendants' addition of two new exhibits as part of Dr. Xu's testimony. Tr. 10-117:1-7; *see* TX-YE and TX-YF.

sought to downplay the significance of their "data mixup" and "mislabeling" (Tr. 11-68:8-12), but it is undeniable that during and after the collaboration ended, they continued to rely on Astellas' HB-MSC technology to advance their T-MSC work and the commercial prospects of ImStem.

5. Astellas Was Injured By Defendants' Unfair Trade Practices

59. Astellas' was injured by Defendants' unfair trade practices. Although the parties' experts disagreed upon the correct methodology to value this harm, both agreed that Defendants did not pay Astellas for the value they obtained from early and detailed access to Astellas' HB-MSC method, cells, and data. Tr. 5-24:19-23, 9-24:3-12.

60. Astellas' expert, Dr. Bell, calculated the value of Defendants' unauthorized use of Astellas' confidential materials and information as the value accrued in ImStem as of the time Astellas' patent application was published in June 2013. Tr. 5-31:17-32:4. Prior to this publication, Astellas should have retained all of the commercial value of their own confidential materials and information. Tr. 5-31:5-16. But because of Defendants' unfair trade practices, Defendants established a competitor, solicited investments, obtained grant funding, and jump-started their own T-MSC program—all based on Astellas' confidential technology. *See* ¶¶ 45-58; Tr. 5-29:25-31:2. Defendants' unfair trade practices enabled them to establish ImStem by June 2013, when they would not have had access to Astellas' technology but for the collaboration. *See* ¶¶ 54-58. Thus, the entire value of ImStem as of June 2013 is a direct measure of the value of the (mis)use of Astellas' technology for which Defendants never compensated Astellas. Tr. 5-31:17-32:4. Using the valuation method endorsed by ImStem's CEO, Dr. Men, Dr. Bell calculated the value of ImStem in June 2013 at $1.6 million. Tr. 5-32:14-33:24, 5-36:5-38:3; TX-BB at -886.

61. Mr. Green took a different approach, using an analysis of certain license agreements to arrive at a hypothetical license fee of $250,000 that, in his opinion, Defendants would have paid Astellas for early and detailed access to Astellas' HB-MSC technology. Tr. 9-34:10-35:5, 9-36:3-

6, 9-83:4-25. However, Mr. Green arrived at this amount using license agreements between related companies and companies who are not competitors. Tr. 9-84:24-85:18, 9-87:3-13. In a more accurate hypothetical license, the fee should be increased in comparison to these agreements because Astellas and Defendants would have been competitors, a situation that increases the licensing terms. Tr. 9-86:20-87:2, 9-87:14-89:3.

III. PROPOSED CONCLUSIONS OF LAW

A. Inventorship

1. Defendants Are Not Co-Inventors On Astellas' '956 and '321 Patents

62. Defendants failed to carry their burden of proving that Dr. Wang and/or Dr. Xu are co-inventors on Astellas' '956 and '321 patents. "Because the issuance of a patent creates a presumption that the named inventors are the true and only inventors, the burden of showing misjoinder or nonjoinder of inventors is a heavy one and must be proved by clear and convincing evidence." *Gen. Elec. Co. v. Wilkins*, 750 F.3d 1324, 1329 (Fed. Cir. 2014).

63. Applicable to all of Defendants' allegations, Drs. Wang and Xu failed to provide credible testimony as to their inventorship claims and corroboration as required by law. "In order to guard 'against courts being deceived by inventors who may be tempted to mischaracterize the events of the past through their testimony,' the law requires corroboration of a putative inventor's credible testimony, the sufficiency of which is measured under a 'rule of reason' standard." *Gen. Elec.*, 750 F.3d at 1330 (quoting *Martek Biosci. Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1374 (Fed. Cir. 2009)); *GemStar-TV Guide Int'l v. Int'l Trade Comm'n*, 383 F.3d 1352, 1382-83 (Fed. Cir. 2004). "[I]n order for the rule of reason requirement to even apply there must be some evidence that a fact-finder can find reasonable; the putative inventor must first provide credible testimony that only then must be corroborated." *Gen. Elec.*, 750 F.3d at 1330 (citing *Univ. of Colo. Found. v. Am. Cyanamid Co.*, 342 F.3d 1298, 1308-09 (Fed. Cir. 2003)); *Univ. of*

Pittsburgh of the Commonwealth Sys. of Higher Educ. v. Hedrick, 573 F.3d 1290, 1298 (Fed. Cir. 2009) (corroboration, preferably contemporaneous, required). At trial Drs. Wang and Xu repeatedly contradicted their statements (some sworn) in contemporaneous documents from the collaboration and their sworn interrogatory responses in this case.[13] *See*, ¶¶ 12, 13, 16-17, 23, 33, 37, 41, 49, 51-58. On these grounds alone, Defendants' co-inventorship claims fail. Without credible testimony and corroboration, Defendants cannot meet their burden of proving by clear and convincing evidence that they contributed to the conception of any of their alleged bases for co-inventorship on Astellas' patents. Defendants' allegations also fail for the reasons below.

a. <u>Using HB-MSCs To Treat MS</u>: Dr. Wang is not a co-inventor on Astellas' '956 patent[14] by contributing the idea of treating MS with HB-MSCs

64. "To be a joint inventor, an individual must make a contribution to the conception of the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention." *Caterpillar Inc. v. Sturman Indus.*, 387 F.3d 1358, 1377 (Fed. Cir. 2004). Defendants failed to prove by clear and convincing evidence that Dr. Wang made a significant contribution to the conception of the claims of the '956 patent by contributing the idea of treating MS with HB-MSCs.

[13] Defendants' suggestion that Drs. Wang and Xu should not be held to the language of their patent applications because of either their inexperience with the patent system or English language proficiency directly contradicts the law requiring corroboration of inventor testimony. In essence, Defendants urge the Court, contrary to law, to give more weight to trial testimony than contemporaneous documentary evidence.

[14] Finding that "[t]here is no excuse for Dr. Xu's lack of diligence in asserting counterclaims related to the '956 Patent," the Court denied Defendants motion to amend their counterclaims to add a claim for Dr. Xu's co-inventorship on the '956 patent. Dkt. 85 at 11. Yet, in their pretrial brief (Dkt. 221 at ¶¶ 120-136) and at trial, Defendants alleged Dr. Xu also contributed to the '956 patent. Astellas maintains that there is no claim for Dr. Xu to be added to the '956 patent in this suit, but refers to Drs. Wang and Xu throughout the '956 patent sections in anticipation of Defendants' arguments. Regardless of whether Dr. Xu could have asserted such a claim, it would fail for the reasons discussed as to Dr. Wang. Moreover, Dr. Xu's lack of diligence and indifference in trying to add such a claim further highlights that Defendants' assertions as to Astellas' patents were purely to gain leverage in this suit, as Dr. Wang admitted (*supra* ¶ 33).

65. Inventorship "requires more than merely exercising ordinary skill in the art—a person will not be a co-inventor if he or she does no more than explain to the real inventors concepts that are well known in the current state of the art." *Caterpillar*, 387 F.3d at 1377 (alterations and citations omitted); *see Gen. Elec.*, 750 F.3d at 1331-32 (contributing idea that was not novel at time of the invention is not sufficient to be named as a co-inventor). "A contribution of information in the prior art cannot give rise to joint inventorship because it is not a contribution to conception." *Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1362 (Fed. Cir. 2004).

66. As set forth above ¶¶ 10-14, MSCs of various types had already shown promise in the laboratory and in clinical trials as treatments for autoimmune diseases, including MS, long before Dr. Wang allegedly suggested this use for HB-MSCs in mid-2010. It cannot be considered a significant contribution to suggest doing with HB-MSCs what others had been doing for years with MSCs isolated from other sources.

67. Defendants suggest their contribution was significant because Astellas' scientists had not yet proven their novel cells were actually MSCs and could not be sure they would work. Tr. 6-46:4-15. But "invention turns on conception, not reduction to practice." *Bard Peripheral Vascular, Inc. v. W.L. Gore & Assocs.*, 670 F.3d 1171, 1201 (Fed. Cir. 2012) *vacated in part on recon.*, 682 F.3d 1003 (Fed. Cir. 2012), *and vacated in part on reh'g en banc*, 476 F. App'x 747 (Fed. Cir. 2012). "An inventor need not know that his invention will work for conception to be complete. [*Price v. Symsek*, 988 F.2d 1187, 1196 (Fed. Cir. 1993).] He need only show that he had the complete mental picture and could describe it with particularity; the discovery that the invention actually works is part of its reduction to practice." *Univ. of Pittsburgh*, 573 F.3d at 1298.

68. In any event, as demonstrated by testimony and corroborating documents at trial, Dr. Lanza was the first to conceive of using HB-MSCs to treat autoimmune diseases, including

MS, and he and Dr. Kimbrel developed the method of making HB-MSCs for that use as well as other uses known in the field for MSCs. *Supra* ¶¶ 1-5. At that time, Drs. Lanza and Kimbrel's conception of using their HB-MSCs to treat diseases in which MSCs were known to be effective, including MS, was complete. They did not need to know with certainty or confirm that their HB-MSCs would be effective in treating MS for their conception to be complete. *Univ. of Pittsburgh*, 573 F.3d at 1298; *Price*, 988 F.2d at 1196. The inventorship analysis does not change in light of Drs. Wang and Xu's argument that they had a "more fully formed idea and more fully formed hypothesis in [their] head," albeit later in time. This is uncorroborated, interested testimony from purported co-inventors, it is legally insufficient to prove co-inventorship. *Gen. Elec.*, 750 F.3d at 1330; *GemStar-TV Guide*, 383 F.3d at 1382-83; *Burroughs Wellcome Co. v. Barr Labs.*, 40 F.3d 1223, 1228 (Fed. Cir. 1994); *Price*, 988 F.2d at 1196; *Univ. of Pittsburgh*, 573 F.3d at 1298. Likewise, Dr. Wang's effort to rewrite his own statements confirming that MSCs were viewed as promising potential therapies for autoimmune disease and MS (*supra* ¶ 12) would fail for lack of corroboration even if it were credible.

69. While Astellas later entered into the collaboration with Drs. Wang and Xu to have them verify that Astellas' HB-MSCs worked in an animal model (EAE) for MS in which MSCs had been proven to be clinically effective, this is also insufficient for inventorship. *Supra* ¶¶ 6-15. "Confirmatory testing or screening of compounds does not constitute a contribution to conception, but is considered reduction to practice." *Intercept Pharm. v. Fiorucci*, 277 F. Supp. 3d 678, 683 (D. Del. 2017) (citing *Burroughs Wellcome*, 40 F.3d at 1229-30 and *Applegate v. Scherer*, 332 F.2d 571, 573-74 (C.C.P.A. 1964)); *Stern v. Trustees of Columbia Univ. in City of New York*, 434 F.3d 1375, 1378 (Fed. Cir. 2006) (conducting animal studies verifying the inventor's conceived use of a novel compound to treat a disease is also insufficient for co-inventorship).

70. Likewise, there was nothing inventive about Defendants testing of HB-MSCs in the EAE model. At best, Defendants "merely assist[ed] the actual inventor after conception of the claimed invention," which does not qualify one as a joint inventor. *Eli Lilly*, 376 F.3d at 1359; *Intercept Pharm.*, 277 F. Supp. 3d at 684 (citing *Burroughs Wellcome*, 40 F.3d at 1229-30 and *Applegate*, 332 F.2d at 573-74); *Stern*, 434 F.3d at 1378.

71. While performing such verification experiments is important in the drug development process, it is not sufficient to render one a co-inventor under the law. *Intercept Pharm.*, 277 F. Supp. 3d at 683 (citing *Burroughs Wellcome*, 40 F.3d at 1229-30 and *Applegate*, 332 F.2d at 573-74); *Stern*, 434 F.3d at 1378. Thus, Drs. Wang and Xu cannot be co-inventors on the '956 patent for this reason and they failed to prove so by clear and convincing evidence, as the law requires. *Gen. Elec.*, 750 F.3d at 1329.

72. The fact that Drs. Wang and Xu are co-authors on a joint publication with the Astellas inventors concerning HB-MSCs is also not relevant. Authorship on a scientific paper "by itself does not raise a presumption of inventorship." *In re Katz*, 687 F.2d 450, 455 (C.C.P.A. 1982). An alleged inventor's being listed as a first author at most shows that he had a substantial involvement in the collaboration, "but can neither prove nor disprove that he contributed to the specific idea of" the claimed feature. *Meng v. Chu*, 643 F. App'x 990, 996 (Fed. Cir. 2016). This legal maxim is illustrated as well by both Defendants and Plaintiffs other scientific publications, which included co-authors who were not named on associated patent filings. *Supra* ¶ 7.

b. <u>Low IL-6 Secretion</u>: Dr. Wang is not a co-inventor on Astellas' '956 patent (or the '551 patent) by suggesting screening for low IL-6 secretion by HB-MSCs

73. Defendants alleged contribution of the idea of screening for low IL-6 production also fails for insignificance compared to what was already known in the field. IL-6 was a well-known immunomodulating cytokine secreted by MSCs, investigating IL-6 levels of MSCs was

commonly done, and the link between IL-6 levels and EAE and MS published years earlier. *Supra* ¶ 17. Merely "explain[ing] to the real inventors concepts that are well known in the current state of the art" does not make one as a co-inventor. *Burroughs Wellcome*, 40 F.3d at 1227-28 (original alterations and citations omitted); *Gen. Elec.*, 750 F.3d at 1331-32; *Eli Lilly*, 376 F.3d at 1362.

74. Defendants' co-inventorship claims based on low IL-6 fail for other, fundamental reasons as well. First, Defendants admitted that low IL-6 is "not independently inventive" in sworn interrogatory responses that were also signed by Defendants' counsel in March 2019. *Supra* ¶ 16. Defendants only changed their position as a litigation tactic to gain leverage in this suit, as Dr. Wang candidly admitted. Tr. 6-265:18-266:2. Second, as Dr. Xu admitted, the level of IL-6 secretion is an inherent property of the cells—nothing need be done to the HB-MSCs to make them secrete low levels of IL-6. *Supra* ¶ 17. Third, while Defendants characterize their idea as "screening" cells for low IL-6, the '956 patent says nothing about "screening." Rather, the claims recite a method of making HB-MSCs that results in cells expressing less IL-6 than BM-MSCs. TX-2 at claim 9(f). Thus, Defendants can't have contributed the "screening" idea to the claims because it isn't in the claims at all. Fourth, the fact that IL-6-related experiments are in the joint publication (TX-9) is irrelevant. It is undisputed that this work was all done ***after*** Dr. Kimbrel had already discovered the low IL-6 secretion property of HB-MSCs and conceived of using it as a marker for therapeutic efficacy. *Supra* ¶ 19. At best, any additional IL-6 work simply confirmed what Dr. Kimbrel had already figured out. "[O]ne does not qualify as a joint inventor by merely assisting the actual inventor after conception of the claimed invention." *Eli Lilly*, 376 F.3d at 1359.

75. Fifth, Defendants' implication that the low IL-6 feature must be inventive because it was included in a dependent claim contradicts their prior, sworn interrogatory responses—signed by their counsel—that dependent claims can, and in the '551 patent do, "recite additional useful,

but not independently inventive features." *Supra* ¶ 16. Defendants' implication is also contrary to law—limitations recited in dependent claims are not, by definition, independent inventive features. *Natron*, 558 F.3d at 1358 ("a dependent claim adding one claim limitation to a parent claim is still a claim to the invention of the parent claim, albeit with the added feature; it is not a claim to the added feature alone"). A person "does not necessarily attain the status of co-inventor by providing the sole feature of a dependent claim." *Id.* at 1358-59 (citing *Hess v. Adv. Cardiovasc. Sys.*, 106 F.3d 976, 981 (Fed. Cir. 1997) as holding "Hess was not a co-inventor, even though he supplied 'heat-shrinkable plastic,' which was the only additional limitation recited in dependent claim 12").

76. Defendants argue (without any expert testimony) their alleged IL-6 contribution is the same in kind as that made by Dr. Nicholas Kouris, a named inventor on Astellas' patents. This is legally irrelevant to the issues before the Court, as issues concerning the named inventors' conception or inventorship are irrelevant "where [the alleged inventor] did not plead any challenge to the named inventors' inventorship." *Tavory v. NTP, Inc.*, 297 F. App'x 976, 981 (Fed. Cir. 2008). In *Tavory*, the Federal Circuit held that the unpleaded defects in the named inventors' conception or inventorship were irrelevant to prove Tavory's inventorship. *Id.* Defendants' suggestion that the Court determine inventorship by comparing Drs. Wang and Xu's contributions to Dr. Kouris's is an invitation to error. In any event, the record does not support their assertion. While Defendants argue that Dr. Kouris's only contribution to Astellas' patents was identifying the expression level of a particular cell surface marker, CD10, the evidence does not show that—and certainly not clearly and convincingly. Defendants likely will rely on a single question and answer from Dr. Kimbrel's deposition. This omits the multiple times that Dr. Kimbrel explained that she is not a lawyer and did not make inventorship determinations. *See, e.g.*, Tr. 2-90:16-21, 2-105:5-13, 2-115:4-116:16, 2-125:4-9. It also ignores Dr. Kouris's testimony that more of his work

is in Astellas' patents than just that on CD10, and that Dr. Kouris brought a wealth of MSC experience to his work at Astellas, having done his graduate dissertation work on MSCs and their use as clinically relevant therapies. Tr. 5-111:21-112:3, 5-112:20-23, 5-115:6-12, 5-116:4-120:1.

77. In any event, even if screening for low IL-6 secretion was inventive (it was not), Dr. Kimbrel was the first to determine that HB-MSCs secreted lower IL-6 than BM-MSCs and that this lower IL-6 secretion could indicate the efficacy of those HB-MSCs. *Supra* ¶ 19. Defendants do not and cannot contest that Dr. Kimbrel performed her IL-6 experiments and determined the low secretion levels of HB-MSCs before them. Instead, Defendants attack Dr. Kimbrel as a scientist, claiming that she "ignored" the data (Tr. 6-92:9-17) and didn't find that the IL-6 was low until after they explained it to her (Tr. 10-101:18-102:12), implying that she may not have actually performed the work despite documents proving the contrary (Tr. 6-222:8-13). These attacks do not come close to clear and convincing evidence that Defendants—not Dr. Kimbrel—first conceived of testing for low IL-6 secretion in HB-MSCs.

c. <u>Mitotically Inactivating HB-MSCs</u>: Dr. Wang is not a co-inventor on Astellas' '956 patent and Drs. Wang and Xu are not co-inventors on Astellas' '321 patent (or the '551 patent) by suggesting to mitotically inactivate HB-MSCs

78. Defendants' alleged contribution of suggesting to mitotically inactivate HB-MSCs, like their other alleged contributions, also fails for lack of significance compared to what was already known in the field. The prior art taught that MSCs that had been mitotically inactivated (irradiated) kept their immunomodulatory effects, as MSCs were known to exert their effects largely by secretion. *Supra* ¶ 21. Further, the prior art taught that hESC-derived cell therapeutic products should be mitotically inactivated for safety reasons, to prevent the risk of tumor formation. *Supra* ¶ 22. Defendants' expert, Dr. Bunnell, even testified that regulatory agencies like FDA would require mitotic inactivation of hESC-derived products for precisely this reason. *Supra* ¶ 22. He further testified that a skilled artisan would know how to titrate the dose of radiation used

to mitotically inactivate MSCs, while maintaining their ability to secrete cytokines and other factors. *Supra* ¶ 22. Thus, everything Defendants allege to have conceived of regarding mitotic inactivation was already known in the prior art. Once again, merely "explain[ing] to the real inventors concepts that are well known in the current state of the art" does not qualify one as a co-inventor. *Burroughs Wellcome,* 40 F.3d at 1227-28 (original alterations and citations omitted); *Gen. Elec.,* 750 F.3d at 1331-32; *Eli Lilly*, 376 F.3d at 1362.

79. This conclusion is consistent with Defendants' sworn interrogatory responses (co-signed by counsel) admitting mitotic inactivation, specifically irradiation, is "not independently inventive." *Supra* ¶ 23. Again, Defendants only changed their position to gain leverage in this suit, as Dr. Wang candidly admitted. Tr. 6-265:18-266:2. Defendants' book chapter also admits that, based on the scientific literature at the time, it was known that MSCs worked through their secretions and thus mitotically inactivated MSCs should work therapeutically. *Supra* ¶ 23. Simply put, the idea to mitotically inactivate hESC-derived cells, including MSCs was known in the prior art and cannot be the basis for a co-inventorship claim. Defendants have not proven by clear and convincing evidence that mitotic inactivation is sufficient for inventorship on Astellas' patents.

d. <u>Comparing HB-MSCs To BM-MSCs</u>: Dr. Wang is not a co-inventor on the '956 patent and Drs. Wang and Xu are not co-inventors on the '321 patent (or the '551 patent) by suggesting to compare HB-MSCs with BM-MSCs

80. Once again, Defendants' alleged contribution, this time suggesting to compare HB-MSCs with BM-MSCs, fails for lack of significance compared to what was known in the art. Comparing new types of MSC with the "gold standard" BM-MSCs was well-known in the art. *Supra* ¶ 24. Dr. Xu even testified such comparisons, using ES-MSCs and BM-MSCs, was "very common" and agreed that it is "what a scientist would naturally do in the situation." *Supra* ¶ 24. Such a common, routine activity cannot be a basis for a co-inventorship claim as inventorship "requires more than merely exercising ordinary skill in the art—a person will not be a co-inventor

if he or she does no more than explain to the real inventors concepts that are well known in the current state of the art." *Burroughs Wellcome,* 40 F.3d at 1227-28 (alterations and citations omitted); *see also Gen. Elec.*, 750 F.3d at 1331-32; *Eli Lilly*, 376 F.3d at 1362.

2. Defendants Are Not Co-Inventors On The '551 Patent

81. At trial, Astellas proved by clear and convincing evidence that Drs. Wang and Xu are not co-inventors of the '551 patent.[15] Astellas demonstrated that the significant invention described and claimed in the '551 patent, considered as a whole, is the HB-MSC method and resulting cells that Drs. Lanza and Kimbrel developed. *Supra* ¶¶ 25-31, 41. This is consistent with the Court's summary judgment decision, which held that Defendants have no factual basis to dispute that Drs. Kimbrel and Lanza contributed to the conception of the invention or that they made a significant contribution to the invention. Dkt. 163 at 8-9. Astellas further proved that Defendants alleged contributions to the conception of certain features claimed in the '551 patent were known in the art, routine for the ordinarily skilled artisan, and insignificant in comparison to the invention as a whole. *Supra* ¶¶ 25-44.

a. Serum-Free And Feeder-Free Culture Of hESCs Was Routine

82. Astellas proved that serum-free and feeder-free culture of hESCs was well-known and routinely performed by skilled artisans before Defendants allege to have conceived of it. *Supra* ¶¶ 32-40. Indeed, this was undisputed at trial. Dr. Xu admitted that serum-free and feeder-free systems were well-known before 2010 and as evidenced in scientific articles from Dr. Lanza's and Dr. Thomson's groups published in 2005 and 2006, respectively. *Supra* ¶ 35. While Defendants testified that Dr. Kimbrel only used feeder cells to culture hESCs when she first made HB-MSCs, she explained that she knew how to culture hESCs feeder-free but chose for business purposes to

[15] The parties also stipulated that this Court's rulings as to the '551 patent would apply equally to the continuation patent Defendants filed, U.S. Patent No. 10,557,122. Dkt. 95.

use feeders, and that other individuals at Astellas at the time were culturing hESCs in serum- and feeder-free conditions. *Supra* ¶ 35. Dr. Brivanlou explained why such a business decision makes sense, as reagents used to culture hESCs in serum- and feeder-free conditions are expensive, so many scientists use serum and feeders during early research stages. *Supra* ¶ 35. Defendants did not rebut this evidence with any counter-evidence. In fact, Dr. Xu agreed Dr. Thomson's group's 2006 paper described how to use the particular mTeSR culture media Defendants used for some experiments in the '551 patent when culturing hESCs serum- and feeder-free. *Supra* ¶ 35. Again, merely "explain[ing] to the real inventors concepts that are well known in the current state of the art" does not qualify one as a co-inventor. *Burroughs Wellcome,* 40 F.3d at 1227-28 (original alterations and citations omitted); *Gen. Elec.*, 750 F.3d at 1331-32; *Eli Lilly*, 376 F.3d at 1362.

b. Using A GSK3 Inhibitor, Specifically BIO, At 0.05-0.2 µM Was Known

83. Defendants' alleged contribution of using a concentration of 0.05-0.2 µM of a GSK3 inhibitor, specifically BIO, cannot be a significant contribution warranting inventorship when this feature was known. Astellas proved by clear and convincing evidence that use of a GSK3 inhibitor, specifically BIO, at 0.05-0.2 µM to culture hESCs in serum- and feeder-free conditions was known before October 2010, when Defendants first began working with it. *Supra* ¶¶ 32-44. Astellas' expert, Dr. Brivanlou, testified about his work discovering the GSK3 inhibitor BIO and how he reported in numerous publications that a minimal concentration of BIO, including those in the '551 patent, could be used to culture hESCs in feeder- and serum-free conditions. *Supra* ¶¶ 37-38. Dr. Brivanlou also explained how Dr. Wang's work, years after his own, replicated what he had shown and tracked his published instructions. *Supra* ¶¶ 37-38.

84. Astellas also proved that both the '551 patent (*supra* ¶¶ 26-31) and Defendants' contemporaneous documents (*supra* ¶¶ 39, 41) show Defendants did not consider GSK3 inhibitor use to be significant. The '551 patent specification and its prosecution history indicate Astellas'

HB-MSC method is the significant inventive contribution. *Supra* ¶¶ 25-31, Even when rarely mentioned, the '551 patent specification and prosecution history filings show that use of a GSK3 inhibitor is optional. *Supra* ¶¶ 26-31. As such, the GSK3 inhibitor feature cannot warrant inventorship because it is insignificant when, as here, the specification and claims primarily focus on the significant invention, and the specification mentions the alleged contribution only rarely. *Nartron Corp. v. Schukra U.S.A., Inc.*, 558 F.3d 1352, 1357-58 (Fed. Cir. 2009).

85. Consistently, aside from mentions in Dr. Wang's lab notebook around October 2010 and a reference to GSK3 inhibitors in a section of his April 2011 presentation on making hematopoietic stem cells, not MSCs, Defendants did not mention using a GSK3 inhibitor in their grants, business plans, or patent applications until years later, in 2013, and even when they finally mentioned it, they stated it was optional. *Supra* ¶ 39. Moreover, Dr. Wang's April 2011 presentation indicates a GSK3 inhibitor was not necessary in order to efficiently make HB-MSCs or yield a substantial number of them, as it relies on Dr. Kimbrel's data, including her data on efficiency and yield that was generated without use of a GSK3 inhibitor. *Supra* ¶ 41.

86. Defendants largely do not dispute what these contemporaneous documents say. Instead, Defendants argue, based on their own trial testimony and that of their expert, Dr. Perry, they used a GSK3 inhibitor for a different purpose than Dr. Brivanlou. *Supra* ¶ 36. As the '551 patent shows, Defendants' litigation-contrived arguments are wrong. The '551 patent explains that Defendants used a GSK3 inhibitor for the exact same purpose as did Dr. Brivanlou—to maintain hESCs in feeder-free, serum-free culture conditions. *Supra* ¶ 36. Moreover, Dr. Wang's April 2011 presentation shows that Defendants' litigation-created claim that they used a GSK3 inhibitor to differentiate hESCs towards MSCs is incorrect. The only discussion of using a GSK3 inhibitor in this presentation was in the first section, on making ***hematopoietic stem cells, not MSCs***. *Supra* ¶

39. Separately, Dr. Perry's testimony should be given no weight at all as his opinions were completely divorced from the facts and evidence because Defendants withheld their internal documents and other materials from him. *Supra* ¶ 40. Defendants' choice led to the absurd outcome where Dr. Perry's testimony that a GSK3 inhibitor is ***required*** in order to achieve a therapeutically effective HB-MSC directly contradicted that of Dr. Wang, who testified that the final product HB-MSCs "work the same" as those made without use of a GSK3 inhibitor. *Supra* ¶ 40.

87. Defendants claim that the GSK3 inhibitor feature must be inventive because it is the only thing explicitly mentioned in the Examiner's Reasons for Allowance also fails. As Astellas proved at trial, the Examiner failed to search the prior art for publications on GSK3 inhibitors and, had he done so, he should have uncovered Dr. Brivanlou's patent publication that disclosed use of the GSK3 inhibitor BIO in a concentration range that overlaps with that in the '551 patent. *Supra* ¶¶ 42-44. Further, Defendants patent law expert, Dr. Zerhusen, admitted that had the Examiner found Dr. Brivanlou's patent publication, he should have rejected the claims as obvious according to the MPEP examination rules, which are based on Federal Circuit law. *Supra* ¶¶ 42-44. A "*prima facie* case of obviousness typically exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art." *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003). Where "the claimed ranges are completely encompassed by the prior art, the conclusion is even more compelling than in cases of mere overlap" because the "normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." *Id*. at 1330. This principle is shown by the fact that Dr. Wang achieved his "exciting" result with a lower GSK3 inhibitor concentration with just two experiments over 10 days. *Supra* ¶ 37. Thus, the Examiner's Reasons for Allowance cannot show that the GSK3 inhibitor feature was

a significant contribution to the '551 patent as the he did not consider key prior art references—Dr. Brivanlou's 2006 and 2009 publications—that demonstrate that this feature was known.

B. Unfair Trade Practices – Chapter 93A

1. Defendants Committed Unfair Trade Practices

88. Defendants committed unfair or deceptive acts by misappropriating Astellas' technology under the guise of an academic collaboration and misusing Astellas' technology for commercial gain. In deciding whether a practice violates Chapter 93A, courts look to "(1) whether the practice is within at least the penumbra of some common-law, statutory or other established concept of unfairness; (2) whether it is immoral, unethical, oppressive, or unscrupulous; [and] (3) whether it causes substantial injury to consumers (or competitors or other businessmen)." *Mass. Eye & Ear Infirm. v. QLT Phototherа.*, 552 F.3d 47, 69 (1st Cir. 2009), *decision clarified on denial of reh'g*, 559 F.3d 1 (1st Cir. 2009) ("*MEEI II*"); *see* Mass. Gen. Laws ch. 93A, §§ 2, 11. Massachusetts courts evaluate unfair and deceptive trade practice claims based on the circumstances of each case. *Id.* (citing *Kattar v. Demoulas*, 739 N.E.2d 246, 257 (2000)).

89. Defendants' unfair conduct, discussed *supra* ¶¶ 45-58, is particularly egregious. As Defendants admitted in contemporaneous documents, they filed the '551 patent as an "attack patent" to "prevent [Astellas] from using their technology to go to clinic and develop product" and to "ask for royalty from [Astellas] if they have successfully marketing [sic] their product." *See, e.g., supra* ¶¶ 31, 47-49. At trial, Dr. Wang admitted he really meant "attack patent"—testifying that he meant to use it as a "bargaining chip" against Astellas in "future litigation." *Supra* ¶¶ 31, 47. This behavior was not even close to within any normal realm of scientific norms and practices (*supra* ¶ 49), and it certainly was "within at least the penumbra of some common-law, statutory or other established concept of unfairness," to which Chapter 93A attaches. *MEEI II*, 552 F.3d at 69.

90. Defendants' misuse of Astellas' confidential information to file patents, solicit

business and investors, seek and obtain grants, and jump-start their T-MSC work constitutes an unfair trade practice under Chapter 93A. Misuse of confidential information, as Defendants did here, supports Chapter 93A liability. *MEEI II*, 552 F.3d at 71; *see also MEEI II clarified on denial of reh'g,* 559 F.3d at 3 (defendant's "liability flows from its less than savory business practices rather than its reliance on public domain sources of information"). Defendants repeatedly promised to keep confidential and not to misuse Astellas' information and materials. *Supra* ¶ 45. These false promises induced Astellas to detrimentally rely on them to continue to supply materials and technical know-how to Defendants over the years to further what appeared, at the time, to be a collaboration. Yet, Defendants in fact treated Astellas as a "major competitor" instead of a collaborator, including Astellas' confidential information in patent filings, grant applications, business plans, and investor presentations, and relying on Astellas' technology to jump start their T-MSC work for commercial gain. *Supra* ¶¶ 45-59. Such "stringing along" of a counterparty—even a sophisticated one—to induce detrimental reliance violates Chapter 93A. *MEEI II*, 552 F.3d at 70 (citing *Greenstein v. Flatley*, 474 N.E.2d 1130, 1133 (1985)).

2. Defendants' Unfair Trade Practices Injured Astellas

91. Defendants' unfair trade practices injured Astellas by Defendants' taking Astellas' HB-MSC technology and using it for their own, unauthorized gain without paying Astellas for the value they obtained. *Supra* ¶¶ 59-61. By repeatedly promising confidentiality and limited use, Defendants extracted more cells and information from Astellas, using it as a payment-free license to Astellas' HB-MSC technology. In *MEEI II*, the First Circuit affirmed liability under Chapter 93A where, as here, the injury included that the defendant "either would not have had a successful product, or would have had to expend considerably greater sweat and treasure to bring [the product] to market" had it not misused the plaintiff's confidential information. 552 F.3d at 70-71.

92. Both parties' experts agreed that Defendants did not pay Astellas for the value they

obtained from this unauthorized use of Astellas' confidential information and HB-MSCs. *Supra* ¶ 59. While the experts disagreed as to the appropriate method to use, Dr. Bell's analysis, which used a valuation method endorsed by ImStem's CEO (*supra* ¶ 60), did not suffer the methodological failings of Defendants' expert, Mr. Green, who used licenses between related companies and companies that were not competitors to arrive at an unrealistically low licensing fee. *Supra* ¶¶ 60-61. Astellas proved the value of Defendants' misuse of Astellas' confidential materials and information is $1,600,000. *Supra* ¶ 60.

93. Astellas also proved Defendants willfully and knowingly committed these unfair trade practices, which warrants multiple damages under Chapter 93A. Mass. Gen. Laws ch. 93A, § 11. Astellas proved that, from the outset Defendants filed the '551 patent as an "attack patent" (*see, e.g.*, *supra* ¶¶ 31, 47-49), and that Defendants willfully and knowingly committed unfair trade practices by repeatedly hiding Astellas' role from their business partners and investors, their previous employer UConn, the State of Connecticut grant funding agency, and the Patent Office. *See, e.g.*, *supra* ¶¶ 48-52. Such "callous and intentional violations of" Chapter 93A "warrant multiple damages." *RGJ Assocs., v. Stainsafe, Inc.*, 338 F. Supp. 2d 215, 238 (D. Mass. 2004).

94. In addition to monetary damages and the enhanced and punitive damages permitted by Chapter 93A, Astellas is entitled to equitable relief. Mass. Gen. Laws ch. 93A, § 11 ("the court shall award such other equitable relief, including an injunction, as it deems to be necessary and proper"). This equitable relief includes an order that Defendants immediately transfer to Astellas all right, title, and interest in all information, patent applications, patents, technology, products, and other materials in their possession, custody, or control that wrongfully constitute, contain, were based on, and or derived in whole or in part from the use of Astellas' HB-MSC technology, as well as an order for a constructive trust over such information, patent applications, patents,

technology, products, and other materials.

3. Defendants' Defenses To Astellas' Unfair Trade Practices Claim Fail

95. Defendants also failed to prove their affirmative defenses of statute of limitations and that their bad acts were insufficiently tied to Massachusetts.

96. Defendants' statute of limitation defense is meritless. The statute of limitations for an unfair trade practices claim under Chapter 93A is four years. Mass. Gen. Laws ch. 260, § 5A. Because Astellas filed suit on November 13, 2017, the trigger date for the statute of limitations is November 13, 2013. The "discovery rule" applies in Chapter 93A actions, where a cause of action accrues "when a plaintiff discovers, or any earlier date when she should reasonably have discovered, that she has been harmed or may have been harmed by the defendant's conduct." *Astellas Inst. For Regen. Med. v. ImStem Biotech.*, 458 F. Supp. 3d 95, 106 (D. Mass. 2020) (quoting *Bowen v. Eli Lilly & Co.*, 408 Mass. 204, 205-06 (1990)). As Defendants' admitted in their summary judgment motion, a plaintiff on inquiry notice may only be charged "with the knowledge of what he or she ***would have uncovered*** through a reasonably diligent investigation." Dkt. 135 at 12 (quoting *McIntyre v. United States*, 367 F.3d 38, 52 (1st Cir. 2004)). Here, the first hint that Astellas had of one of Defendants' unfair acts was in February 2014, when it first saw Defendants' PCT application on Astellas' HB-MSC technology. Dkt. 113 at ¶ 62. This is unquestionably after the trigger date for the statute of limitations. Moreover, this hint—at most—was only to one of Defendants' bad acts that form the basis for Astellas' claim. It revealed nothing about how Defendants founded ImStem on Astellas' HB-MSC technology, used Astellas' technology to seek grants and investments in ImStem, or used Astellas' HB-MSC technology to jump start their work with T-MSCs. As the First Circuit has clarified, the limitations period does not start if the plaintiff does not know "the full extent of its claim," as is the case here. *Mass. Eye & Ear Infirm. v. QLT Photothera.*, 412 F.3d 215, 241 (1st Cir. 2005) ("*MEEI*").

97. To the extent Defendants argue Dr. Kimbrel's concerns about "scope creep" somehow show Astellas had inquiry notice earlier, that assertion is also meritless. Dr. Kimbrel explained that when she was concerned, she sent Defendants several emails seeking their repeated agreement to keep Astellas' materials confidential and to only use them for limited purposes. Each time Defendants agreed to Dr. Kimbrel's terms, which reassured her. Tr. 2-60:4-17, 2-61:7-13. In other words, Dr. Kimbrel ***investigated*** her concerns by seeking reassurances from Defendants that they were not improperly disclosing or using Astellas' technology. Each time, Defendants' agreed to those terms. Dr. Kimbrel could not have known that Defendants were lying, or the extent of their misuse and disclosure of Astellas' technology, as Defendants actively concealed it from her. As Astellas explained in its summary judgment opposition, Defendants' fraudulent concealment of their wrongful uses of Astellas' technology tolls the statute of limitations under Mass. Gen. Laws ch. 260, § 12. Dkt. 142 at 7-10.

98. Separately, the statute of limitations is not applicable because Defendants' bad acts are continuing torts. A continuing tort that tolls the statute of limitations arises not by continuing ill effects from an original tort but by continual unlawful acts. *Maslauskas v. United States*, 583 F. Supp. 349, 351 (D. Mass. 1984). Even though Defendants' PCT patent filing became public in 2014, the First Circuit has rejected that "in a complex case of this nature—where trade secrets of varying importance are alleged to have been divulged over a period of years—that notice of one misappropriation can constitute sufficient notice to begin tolling the statute for all misappropriations." *MEEI*, 412 F.3d at 240. A wronged party like Astellas "should not be prejudiced with regards to later torts committed against it, simply because a defendant started the clock running by committing similar acts at an earlier time." *Id*. at 241.

99. Defendants' assertion that their unfair business practices "primarily and

substantially" occurred outside of Massachusetts also fails. Defendants failed to meet their burden to establish that the accused actions did not occur primarily and substantially within Massachusetts. *RGJ Assocs.*, 338 F. Supp. 2d at 233. In fact, Astellas demonstrated that the "center of gravity" of the accused activities are primarily and substantially in Massachusetts. Astellas demonstrated that it was injured in Massachusetts. *See* ¶ 59. Further, Defendants sent deceptive and misleading communications to Astellas in Massachusetts, falsely promising to maintain Astellas' materials and technology as confidential and inducing Astellas to share its valuable confidential materials that were developed in Massachusetts. *See* ¶¶ 45-58. Indeed, Defendants traveled to Massachusetts to procure Astellas' cells and protocol under these false pretenses. Tr. 6-155:20-156:4. Defendants further incorporated these Massachusetts-developed materials and information in their "attack patent" and in grant applications on Astellas' technology and business plans to establish a direct competitor to Astellas. *See* ¶¶ 47-48, 51-58. Such activities evidence that Defendants cannot prove they did not occur primarily and substantially in Massachusetts. *See, e.g.*, *Pavonix, Inc. v. Barclays Bank PLC*, 2015 WL 9243831, at *11 (D. Mass. Nov. 25, 2015) (alleged misrepresentations "were received primarily in Massachusetts" and their impact was felt there); *RCJ Assocs.*, 338 F. Supp. at 236-37 (alleged unfair activities occurred primarily in Massachusetts where defendant sent misleading communications to Massachusetts where plaintiff acted upon them, the products at issue had been manufactured exclusively there, and plaintiff "learned of and incurred the loss in Massachusetts"); *Sentinel Prod. Corp. v. Mobil Chem. Co.*, 2001 WL 92272, at *24 (D. Mass. Jan. 17, 2001) (alleged misconduct could be found to have occurred primarily and substantially in Massachusetts because the Massachusetts-based plaintiff suffered losses there, defendant sent employees there to inspect machine and obtain specifications, and plaintiff drafted purchase order in Massachusetts in response to defendant's misrepresentations).

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CERTIFICATE OF SERVICE

I hereby certify that this document, which was filed with the Court through the CM/ECF system, will be sent electronically to all registered participants as identified on the Notice of Electronic Filing, and paper copies will be sent on December 4, 2020 to those identified as non-registered participants.

/s/ *David P. Frazier*
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